

MINISTRY OF HEALTH

Reports on Public Health and Medical Subjects

No. 101

Rubella and other Virus Infections during Pregnancy

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LONDON

HER MAJESTY'S STATIONERY OFFICE

1960

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PREFACE

Reports from Australia in the early 1940's suggested that congenital malformations occurred in seriously high frequency amongst infants whose mothers had had rubella in the early part of their pregnancy.

Those findings aroused world-wide interest. In this country it was decided that an attempt should be made to ascertain, firstly, the frequency with which the birth of a malformed child followed an attack of rubella or certain other virus diseases during pregnancy and, secondly, the extent to which the occurrence of these diseases during pregnancy increased the normal hazard of bearing a defective child. To this end a *prospective* enquiry on a national scale was designed by the General Register Office, the Ministry of Health and the Department of Health for Scotland and sponsored by the Society of Medical Officers of Health.

All the medical officers of local health authorities throughout England, Scotland and Wales took part. From 1950 onwards they selected the appropriate virus infection cases together with a large series of control cases, and obtained the required information about the expectant mothers and their infants. Their generous co-operation made it possible to carry out the survey on a large scale, and the number of completed cases and controls under review, 7,230, and the general high standard of reporting give an indication of the skill and pertinacity with which the field work was performed. In this they have earned the gratitude of their fellow citizens. The information obtained by the medical officers of health was analysed and studied in the Ministry of Health and the General Register Office. The report which follows embodies the conclusions to be drawn therefrom.

Two important features of the report are (a) the demonstration that the risk of rubella in early pregnancy leading to the birth of a malformed infant is very much less than the original observations indicated but (b), that the occurrence of deafness should be specially looked for in all children born of rubella mothers, and that such children should be kept under medical observation until the possibility of a hearing defect can be excluded.

The other virus infections studied did not have the same deleterious effects on the foetus as did rubella occurring in the first trimester.

While it is apparent that the consequences of rubella infection during pregnancy do not constitute a major factor affecting the public health the effects may be grave for certain infants, though some of the defects such as cataract and congenital deformities of the heart are now amenable to surgery. Other infants manifest some degree of hearing defect ranging from severe to very slight. But the majority of infants born to mothers who have rubella during pregnancy, even in the early months, apparently do not suffer any harm.

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Ministry of Health,
London.
July, 1960.

I. INTRODUCTION

"In the first half of the year 1941 an unusual number of cases of congenital cataract made their appearance in Sydney. Cases of similar type which appeared during the same period have since been reported from widely spread parts of Australia. Their frequency, unusual characteristics and wide distribution warranted closer investigation". So Dr. Norman Gregg opened an address in 1941 in which attention was drawn for the first time to an association between maternal rubella and congenital malformations.

Gregg¹ reviewed a series of 78 infants from different parts of Australia who had congenital cataract of a peculiar type, usually bilateral and obvious from birth as dense white opacities occupying the pupillary area. In his opinion this appearance did not exactly correspond to types of cataract previously described. Most of the infants were small, ill nourished and difficult to feed; 44 of them suffered also from a congenital defect of the heart.

The similarity of the eye defects, the frequency of the accompanying heart defects and the widespread geographical incidence of the cases suggested that they were the result of some constitutional condition of a toxic or infective nature, rather than of a purely developmental defect. The early period of pregnancies under review corresponded with the peak of a very widespread epidemic of rubella in Australia in 1940. Enquiries into the medical history of the mothers during the early months of pregnancy revealed that all but 10 gave a history of rubella, usually during the first or second month of pregnancy. There was also a high incidence of primiparae in the group and these were women who were thought to be most likely to be exposed to and infected with rubella. One woman gave a history of a severe attack of rubella three months before her pregnancy.

Gregg believed that the rubella of the 1940 epidemic in Australia differed greatly from the usual virus infection of that name. It was much more severe and was frequently accompanied by severe complications. He also mentioned the occurrence, during the same period, of epidemics of sore throat, first in military camps and later spreading to the civilian population.

Shortly after Gregg's pronouncement two large-scale investigations were carried out in Australia. In Southern Australia Swan and his co-workers began in 1942 their extensive work in the field. In New South Wales a Committee which included Gregg himself, was appointed in 1944 by the Director General of Health to investigate Gregg's observations. These investigations confirmed and amplified the original findings.

The New South Wales Committee² reported that of 180 congenitally defective children a history of maternal rubella had been revealed in 130 cases and came to the following conclusions:

"1. That the maternal infection was rubella, with possibly an increase in the virulence of the organism.



2. That cases of congenital defects following maternal rubella during pregnancy had occurred previously to 1940, but the relationship between maternal infection and the congenital defect or defects had not been recognised.
3. That it is impossible to estimate the number of pregnant women and subsequent children affected as a result of the epidemic of 1940.
4. That apparently children are not affected when the maternal infection occurs after the fourth month of pregnancy.
5. That the defects noted have been deaf mutism, eye and heart disease, and possibly mental defectiveness, and that the first three defects may occur singly or in any combination.
6. That there is no relationship between the severity of the maternal infection and the nature of the defect in the child.
7. That if the maternal infection occurs after the second month of pregnancy there is less likelihood of eye disease occurring in the child.
8. That a large number of the affected children are below normal average birth weight.
9. That the majority of the children are below average weight for age and that they show a degree of microcephaly and their general physique is generally below standard.
10. That many of the children are late in sitting up and walking and difficulties in feeding are common.
11. That during the first few years of life, signs of general instability of the nervous system of the children are common to most of them.
12. That the deafness is not absolute and the apparent improvement in hearing about the second half of the fourth year is secondary to improvement in the power of concentration at this period.
13. That the main dental abnormality is retardation of eruption, but that at three and a half years all the children had a full complement of teeth.
14. That very few of the children are mentally defective though many are mentally retarded, but that the majority of the children are educable and will be fit to earn their own living, following appropriate education.
15. That there is no evidence to show that the occurrence of rubella during pregnancy has any harmful effects on the mother".

Swan, *et. al*^{3,4,6} published a series of papers giving the results of their investigations in Southern Australia. Altogether, 120 defective children were investigated and in 101 cases rubella had occurred during pregnancy.

In the majority of cases rubella had occurred within the first four months of pregnancy and there was some evidence that the type of defect was related to the time when rubella occurred. Heart and eye defects were most common when rubella occurred in the first and second months, and hearing defects when rubella had been in the second and third months. The rubella children showed abnormalities in the following frequencies: microcephaly, 62 cases; heart disease, 52 cases; deaf-mutism, 48 cases (one child suffered from deafness only); cataract, 18 cases (12 bilateral, six unilateral); mental deficiency, five cases;

strabismus, four cases; cryptorchidism, four cases; inguinal hernia, three cases; spina bifida occulta, three cases; high-arched palate, three cases; and a considerable number of other defects occurring in one or two cases only.

In the 1943 paper³ it is stated that, "On the available evidence, when a woman contracts rubella within the first two months of pregnancy it would appear that the chances of her giving birth to a congenitally defective child are in the region of 100 per cent, and if she contracts rubella in the third month they are about 50 per cent, . . . there is still a slight likelihood that the child will be congenitally defective if rubella is contracted after the third month of pregnancy". In 1946, having found three cases of maternal rubella in the first two months (one in the first and two in the second) followed by normal children, the authors conceded that, "it is possible that rubella in early pregnancies is not invariably followed by congenital defects in the child". They also came to the conclusion that the epidemic disease of 1940 really was rubella, although of a severer type than usual.

Following the publication of the original Australian accounts of an association between maternal rubella during pregnancy and subsequent congenital defects in the child, observers in other countries, notably America, England, Sweden and Holland, reported somewhat similar findings.

The original Australian workers and later observers approached the subject from different viewpoints, according to their own speciality or in a more general way. The ophthalmologist investigated the maternal histories of blind children as Gregg himself did, the otologist started with deaf children, e.g., Carruthers in Sydney⁴, the cardiologist with children with congenital heart disease, e.g., Dogramaci and Green, U.S.A.⁵; the statistician started with the annual national rates of malformation, e.g., Lancaster, Australia^{6,7}. Others collected information about all kinds of malformed children.

In England, Clayton-Jones¹⁰, made a study of deaf children, by means of questionnaires which were sent to the mothers of children in deaf schools. Out of 141 cases 19 mothers gave a history of rubella during pregnancy, which in all cases had been within the first four months.

It is not necessary to record here the individual cases reported and it is impossible to do justice to all the detailed studies. An excellent account of the evidence produced up to the time of its publication is given by Swan in his prize essay "Rubella in Pregnancy as an Aetiological Factor in Congenital Malformed Still births"¹¹. Another comprehensive and erudite review was published by Wesselhoeft¹². It is, however, pertinent to the purpose of this paper to consider the methods used in carrying out these studies.

Practically all the evidence adduced by the early Australian workers and their immediate followers in the field was obtained by retrospective methods. They started with malformed children and then questioned the mothers about the occurrence of rubella during their pregnancies. Such investigations produced valuable information about the association between maternal rubella and certain types of malformation but they could not give an accurate estimate of the frequency with which rubella caused these malformations, nor indicate how much more a mother who had rubella during her pregnancy was likely to have a malformed child than she would be in the normal course of events. The original estimations of this risk were much exaggerated since they were based only upon consideration of the malformed children resulting from pregnancies

complicated by rubella, insufficient consideration being given to the children who were born normal. A fair estimate of the risk could only be obtained by adopting a prospective technique, i.e. by observing, in the first instance, the attack of rubella in a pregnant woman and subsequently examining her offspring. Yet Swan in his prize essay of 1949 made the following statements, "A survey of the available evidence shows that the risk of a mother giving birth to a child with congenital anomalies following the contraction of rubella in the first 4 months of pregnancy ranges from 83.2 per cent in the first month to 61.1 per cent in the fourth month, with an average of approximately 74.4 per cent, whereas in the last 5 months of gestation the risk ranges from 11.1 per cent to 29.2 per cent with an average of approximately 22.8 per cent".

Nor could such retrospective enquiries be relied upon to produce accurate maternal histories. The diagnosis of rubella was based on the mothers' statements. A woman questioned some years after a particular pregnancy would find it difficult to remember an attack of rubella, which at the time might have been merely a minor upset, still more to recall accurately the time in that pregnancy when such an illness had occurred. There is, too, the possibility that the mother of a malformed child, in her anxiety to find a cause for the malformation will, when the suggestion is made to her, remember some slight illness during her pregnancy and identify it as rubella.

Many studies of investigations by the prospective method, starting with a woman known to have had rubella during her pregnancy, have been published.

Fox and Bortin of Milwaukee, U.S.A.¹², reported such a study. During 1942-43 and 1944, 22,226 cases of rubella were reported to the Public Health Department. Of 152 married women who were investigated 11 had rubella during a pregnancy. Only one case suggested a coincident or direct involvement from the disease. Rubella occurred in the first month and the mother had a hydrocephalic still birth. Of the 10 other cases, in four rubella occurred in the first two months, in four during the second to fourth month, in one in the seventh month and one in the ninth month. This gave a completely different picture from the Australian findings and suggested that the risk of rubella producing congenital defects was not so great as had been alleged. The writers concluded that rubella in pregnancy was not, as some observers had suggested, an automatic indication for the termination of pregnancy.

Ober, Horton and Feemster of Massachusetts¹⁴, sent questionnaires to about 3,000 women in the age group 17-49 who had been notified as having had rubella in 1943. Replies revealed that 49 women were pregnant at the time of infection; other methods produced five more cases. The stage in pregnancy when infection had occurred was stated in 52 cases. Of 22 first trimester cases, there were six abortions or still births, five defective and eleven normal children; of the 30 cases in which rubella had occurred later than the third month of pregnancy there were three abortions or still births, two defective and 25 normal children.

Aycock and Ingalls of Boston, Mass. U.S.A.¹⁵, using the same method as Fox and Bortin, investigated 1,300 rubella cases notified to the Board of Health in two Massachusetts communities and found four cases of rubella occurring during pregnancy. In two, infection was in the second month, one baby was normal and one was mentally retarded. In the others infection occurred in the fourth month and the ninth month—both babies were normal. They also followed

up 131 cases of poliomyelitis during pregnancy (27 in the first three months)—92 of the children born were normal; 33 pregnancies ended in abortion or still birth (13 where poliomyelitis had occurred during the first three months of pregnancy); three children had poliomyelitis; another child was "lame"; and two had congenital malformations. In both of these last two cases the attack of poliomyelitis had been in the first three months of pregnancy.

Grönvall and Selander, (Sweden)¹⁶, collected data about the effect on the foetus of certain virus diseases, including rubella in pregnancy.

Women were questioned as to whether and when they had virus infections during pregnancy and 26 reported that they had rubella during pregnancy. Of these 26 mothers, two aborted in the first and third months of pregnancy when rubella occurred. The child of one mother who had rubella during fourth month died during delivery but had no malformation. The remaining 23 mothers produced 25 children, including two twin births, only one of whom was abnormal in having a naevus pigmentosus, (rubella at the fifth month).

The times of infection during pregnancy in the cases of the 24 normal children were: two in first month, five in second month, four in third month, six in fourth month, three in fifth month, two in sixth month, one in seventh month and one in ninth month.

Fox, Krumbiegel, and Teresi¹⁷ investigated six cases of maternal measles (one in the first three months of pregnancy), 23 cases of mumps (six in the first three months), and four cases of chicken-pox (one in the first three months). Only one child had a congenital malformation, hare-lip, following maternal measles in the fourth month of pregnancy. A control series was also studied consisting of 665 children born to 297 women who had had one of these three infectious diseases in 1942-5 before or after but not during pregnancy. Six cases of congenital malformations were discovered in the control series.

Packer¹⁸ reviewed the literature relating to the influence of maternal measles (morbili) on the foetus and reported the results of a postal enquiry that he conducted in South Australia into the outcome of pregnancies complicated by measles. There were seven pregnancies in which measles had occurred during the first three months of pregnancy, and these gave rise to one abortion and two live-born children with congenital malformations. The remainder were normal. Eleven other pregnancies in which measles had occurred after the first three months of pregnancy resulted in one abortion and one still birth, the others being normal.

In England, Bradford Hill and Galloway¹⁹, used National Health Insurance Records of employed women to pin-point cases of virus infection followed by maternity during the course of the next twelve months. Twenty-two complicated pregnancies, ten with rubella, were found and the children were subsequently examined. The authors concluded that although no information of value could be deduced from such small numbers, the method employed was satisfactory and the investigations would continue on a larger scale. Further results published in 1958 are mentioned later in this chapter.

It is generally accepted that the prospective rather than the retrospective type of enquiry gives a more accurate measure of the effect of rubella upon the foetus. It shows that on occasion the foetus might be damaged causing either abortion, still birth or a malformed child. On the other hand there might be no foetal

damage and a normal child be born. But many prospective enquiries can also have limitations. Rubella in adult life is uncommon and the double event of an attack during a pregnancy is even less frequent. Moreover, many of the prospective studies relied on post-natal enquiries about the maternal history. Although a start was made with the pregnant women who had suffered from rubella the child was already born when enquiries began and the outcome was known. A more satisfactory type of true prospective study would start with a pregnant woman who has an attack of rubella and is then kept under observation until pregnancy terminates, the child being examined and thereafter kept under observation for some years. The actual risks involved when rubella occurs during pregnancy can only be estimated by comparing the outcome of pregnancies complicated by rubella with the outcome of uncomplicated pregnancies and this entails the observation of a suitably matched control series of pregnant women.

The investigation which is being described in this report was devised to overcome the deficiency of numbers of cases observed in previous prospective studies and also to provide a control series of pregnancies in which rubella had not occurred. Since its inception in 1950 the results of several other prospective studies have been published.

Brown and Nathan²⁰ published a report of such a study. The city of Manchester, the only area in England and Wales in which rubella is a notifiable disease, experienced its largest recorded epidemic of rubella in 1952 and 28 cases of rubella at various stages of pregnancy were discovered. (At least six of these cases are included in the Ministry of Health investigation). In this series there were five cases of gross abnormality in the children, two of whom were still-born. In addition there was one carneous mole. The proportion of live-born children in Manchester in 1952 known to have congenital abnormality was two per cent.

Lundström²¹ recorded the effects of a 1951 rubella epidemic in Sweden on the pregnancies of women who contracted or were in contact with rubella. The staff of maternity hospitals were asked to question all women delivered in them regarding rubella infection during the current pregnancy. A control series was selected from the women whose case numbers immediately preceded those of selected rubella cases.

From a series of 1,067 rubella cases it was found that when rubella occurred during the first four months of pregnancy the incidence of abnormality which included still birth, neonatal deaths, abnormalities and prematurity was 17 per cent compared with six per cent in the control series.

A higher incidence of abnormality was also found amongst women who had earlier suffered from rubella and had been exposed to infection during the first four months of the current pregnancy but had not contracted the disease.

Infection after the fifth month of pregnancy had no ill effects.

Brawn²² reported that during a mild epidemic in Georgia in 1952, 26 cases of rubella in pregnancy were discovered. Therapeutic abortion was carried out in four cases and the remaining 22 were followed to the end of gestation. Of 15 first trimester rubella cases there were one still birth, four malformed children (malformation of heart, cleft palate and cataract) and 10 normal children. The outcome in 33 per cent of these cases was therefore abnormal. When rubella had occurred later in pregnancy there were no major abnormalities.

Lamy and Seror²², following an epidemic of rubella in Paris in 1953 sent questionnaires to 110,964 women whose pregnancies had been registered at that time. It was found that of 48 women who had rubella during the first four months of pregnancy six aborted, and 24 had congenitally malformed infants. Of those who had rubella during the first seven weeks of pregnancy, 24 in number, four aborted, 19 had defective children and only one had a normal child. From a control group of 571 pregnancies there were eight abortions, 14 infant deaths, one defective child and 548 normal children.

Pitt of Melbourne²⁴ criticised the early Australian estimates of the risk of rubella during pregnancy. They were, he considered, exaggerated and were higher than any suggested by workers in other countries. In his paper he describes a prospective enquiry organised and now being carried out by the Department of Obstetrics and Gynaecology of the University of Melbourne. Doctors notify the Department immediately rubella is diagnosed in a pregnant woman. The diagnosis is confirmed by second opinion. Thereafter observation of the case continues until the child's follow up investigation is completed. He also reviews 20 cases of rubella in pregnancy found over the last eight years in the antenatal department of the Royal Women's Hospital, Melbourne. Of 14 children born to mothers who had rubella before the fourth month three had major malformations: (a) bilateral cataract and microcephaly, (b) megalocornea and heart lesion, (c) cardiac defect. In conclusion he suggests that the true rubella malformation rate is somewhere between 10 per cent and 25 per cent.

Ingalls²⁵ collected from his own and other observers' studies, 100 cases of pregnancies which had been followed up to delivery after a rubella infection had been reported. Sixty-three of the rubella infections occurred in the first trimester: four children were still-born and ten had a congenital defect. Twenty-eight pregnancies in which rubella had occurred in the second trimester yielded two still births and four defective children and nine third trimester pregnancies produced no still births and no defective children.

Greenberg, Pellitteri and Barton²⁶ describe an investigation which began in 1949 in New York City. In the following seven years 233 women who had rubella during pregnancy were followed up to delivery and live children were examined at birth and one year later. Of 103 first trimester rubella pregnancies 48 were terminated by therapeutic abortions, 45 of them because of rubella, and 10 were lost sight of. In the remaining 45 there were 28 normal births, 12 miscarriages, three still births and three malformed children: twins had bilateral cataracts and congenital heart disease and another child had bilateral cataracts and microphthalmus. The mothers of the malformed children had had rubella during the fourth week of pregnancy. Of 89 second trimester rubella pregnancies four were therapeutically aborted and seven were lost sight of. Of the remaining 78 there were 74 normal births, one miscarriage, two still births and one malformed child, who died after 36 hours with Fallot's tetralogy; rubella had been in the 14th week of pregnancy. Three of the 31 third trimester infection cases were lost sight of. Of the 28 remaining, 27 mothers had normal children and one had a still birth.

By adding their results to those of the other prospective investigations the authors found that of 125 first trimester infections there were nine still births and 15 defective children; of 130 second trimester infections there were six

still births and five defective children and of 59 third trimester infections one still birth and no defective children.

Bradford Hill *et al.*²⁷ published further results of the enquiry described in 1949. They recorded a series of 44 cases of rubella in pregnancy. Of 18 first trimester cases there were 13 normal children, one child died unexamined and 4 children had characteristic malformations. One child (rubella 2nd week) had congenital heart disease and bilateral cataracts. The second (rubella 3rd week) had bilateral cataract and microphthalmus. The third (rubella 4th week) had congenital heart disease and severe bilateral deafness and the fourth (rubella 13th week) had partial bilateral deafness.

Of the 15 second trimester cases there were 12 normal children and one who died unexamined, one still birth (rubella 16th week) and one mongol (rubella 14th week).

The five third trimester cases showed no abnormalities. This was also the case with the six cases of rubella infection before the last menstrual period. As the authors themselves state, their mode of enquiry throws no light on the possibility of virus infection causing early foetal death.

As other authors have done, they too, have tabulated their own results with those of three others who worked along similar lines. The tabulation is given below.

*Risk of defect in the infant following maternal rubella during pregnancy.
(Summation of data from four series)*

Stage of Pregnancy at which Rubella commenced					Number of Cases	Infants with Major Defects	
						Number	Per cent
Weeks of Pregnancy	1st-4th	12	6	50
	5th-8th	20	5	25
	9th-12th	18	3	17
	13th-16th	18	2	11
	17th-24th	17	1	6
	25th or later	19	0	0
Total					104*	17	—

* Excluding two cases which terminated in abortion (rubella in the 5th and 12th weeks respectively) and three cases in which the children could not be traced. One pair of fraternal twins (rubella in the 21st week) is included as two cases.

Data were also produced about pregnancies complicated with mumps, 35 cases, chickenpox, 30 cases and measles, 10 cases. There was no evidence that these infections had any deleterious effect upon the foetus except that in the chickenpox cases the proportion of live-born children with low birth weights was relatively high.

II. THE ENQUIRY—ITS INCEPTION, PURPOSE AND METHOD

As indicated in the previous chapter it had become evident by 1950 that an attack of rubella during pregnancy was sometimes followed by a still-born or defective child, but the number of cases so far observed in prospective studies was too small to give any indication of the frequency with which this occurred. In one respect this paucity of numbers was fortunate as it suggested that few pregnant women contract rubella, but only an extensive controlled investigation on prospective lines as described by Logan²⁶ would provide a convincing answer to the question, "What is the risk of a defective baby following an attack of rubella during pregnancy?"

The investigation should begin with the selection of cases of complicated and uncomplicated pregnancies and the attack of rubella should be recorded before the termination of the pregnancy. The diagnosis of the infection should be made by a doctor and the time in pregnancy when it occurred should be accurately stated. The outcome of the pregnancy should be recorded and live-born children medically examined at birth and at intervals for a number of years. A control series of cases of uncomplicated pregnancies should be studied in the same way. A considerable number of virus and control cases would have to be observed in order to provide statistically significant results. All this has been attempted in the present enquiry, the purpose of which is to determine the relative frequency with which congenitally malformed children are born to women who suffer from certain virus infections during pregnancy and to women who have no such infections during pregnancy.

In 1946 a limited pilot survey was undertaken by the Medical Officers of Health of twelve of the larger local health authorities. Expectant mothers attending local health authority ante-natal clinics were questioned as to the occurrence of any illness and mothers who contracted rubella were kept under special observation. In these areas, with a combined population of over 4,000,000 only 15 cases of rubella in pregnancy were found in two and a half years. The time of infection was unknown in five cases. The five first trimester cases produced one miscarriage, one normal child, one child with sclerema neonatorum who died in eight days, one child with multiple deformities who died in a few hours, and one child with bilateral cataracts and congenital heart disease. The four second trimester cases and one third trimester case, had normal children.

No conclusions could be drawn from these few cases but this small survey did show that a forward enquiry in this country would have to be on a national scale, and over a long period, to produce sufficient data from which reliable conclusions could be drawn.

In 1950, at the request of Sir Wilson Jameson, then Chief Medical Officer of the Ministry of Health, the Society of Medical Officers of Health sponsored the present enquiry and all medical officers of local health authorities in England

and Wales and Scotland agreed to take part. The Ministry of Health and General Register Office were responsible for the planning of the enquiry, the provision of record and registration cards and the analysis of the results. Booklets explaining the purpose of the enquiry and containing notes of guidance as to the collection of information were supplied to everyone taking part in it. The method of enquiry was prospective. Pregnant married women who contracted certain virus infections and a control group of pregnant married women who suffered none of these infections were selected as early in pregnancy as possible. The virus infections included rubella, measles, mumps, chickenpox and poliomyelitis.

Medical Officers of Health were responsible for the collection of information in their areas and made what arrangements were necessary. They enlisted the co-operation of general practitioners and the obstetric staffs of maternity hospitals, so that women who were receiving ante-natal supervision from their family doctors and at hospital ante-natal clinics, as well as those attending local health authority clinics, were under review—in fact the majority of pregnant women in the country. From these women two groups of cases were selected.

- (a) "Virus infection cases", women who on first coming under observation had already had one of the virus infections during that pregnancy or who subsequently developed such an infection during the pregnancy.
- (b) "Control cases", were selected from women who on first coming under ante-natal supervision had not suffered from any of the virus infections during that pregnancy. To obtain an adequate number and a representative series of cases each woman whose birthday was stated to be the 31st of any month was selected thus producing a random two per cent sample. If a woman selected as a control case contracted a virus infection later on in her pregnancy she was transferred from the control to the virus group.

Doctors and midwives questioned their ante-natal patients at the first and subsequent examinations as to the occurrence of any illness before or between visits. When a virus infection was reported the date of infection was ascertained and if a doctor had been consulted he was asked for confirmation of the diagnosis and whether the infection was mild, moderate or severe. The information was entered on the mother's record card and the Medical Officer of Health at the same time sent a registration card to the General Register Office. Similarly, whenever an expectant mother was selected as a control case, the Medical Officer of Health registered the case at the General Register Office. As the registration card gave the date on which the case was selected for observation and the record card gave the date of delivery it was possible to ensure that every case had been selected during pregnancy before the birth of the child. Registration cards received at the General Register Office after the date on which the pregnancy ended were rejected even if selection had been before this. No cases already registered were excluded after the birth of the child.

After selection, virus and control cases were kept under observation until the termination of the pregnancy. In the event of abortion, miscarriage or still birth the record card was completed as far as possible and returned to the General Register Office. In the case of live births the children were kept under

Registration Card

SURNAME (in block letters)

Christian Names

Address

Date of Selection

Place of selection (state name of clinic, hospital, etc.)

Ring round

1 if a control, 2 if a virus infection,
3 if a virus infection occurring in a control

If 2 or 3, state diagnosis

Local Health Authority

Expected month of confinement

**MINISTRY OF HEALTH: VIRUS INFECTIONS DURING PREGNANCY
REGISTRATION CARD**

observation for two years, medical examinations being undertaken as soon after birth as possible, at one year and at two years of age by local health authority or hospital medical officers or by the family doctor. After the third medical examination or on the death of the child before 2 years of age, the completed record card was returned to the General Register Office. Inevitably in an enquiry of this size a proportion of the children under observation were lost sight of, mainly due to change of residence. But thanks to the care taken by medical officers of health in transferring record cards from one district to another on change of address only a small proportion of cases was lost.

It was realised that some congenital defects, particularly those of hearing, might not be apparent by two years of age, but it was considered that any advantage gained by extending the period of observation would be out-weighted by the increase in the number of cases lost from sight. A further follow-up could be arranged later if necessary. Indeed a number of children whose mothers had rubella in the early months of pregnancy were examined again when they were between three and six years of age. In London and Middlesex it was possible to arrange for complete paediatric and aural examinations of rubella and similarly matched control children at a central clinic. In the rest of the country examinations were carried out locally and there were no controls. (See Chapter V, Sections I and II).

The first registration card was received at the General Register Office in July, 1950. By the end of December that year 552 registrations and by the end of December, 1951, 4,469 registrations had come in. Scotland entered the Enquiry in April, 1951. By the end of 1952, 8,364 registrations comprising 1,745 virus infection cases and 6,619 control cases had been received. The cases of virus infection included 654 of rubella, 139 of measles, 353 of chicken-pox, 565 of mumps and 34 of poliomyelitis. On 31st December, 1952, the selection of new cases was discontinued, but those cases already selected were kept under

observation for the requisite time. Seven counties and six county boroughs were invited to continue to select cases of rubella in pregnancy for one more year. In these areas 65 cases were registered and followed up, but as they did not come within the scope of the main enquiry they have not been included in the analysis of its results. Details of them are given in the appendix, page 100.

The table below shows how many registered cases were successfully followed up and used in the analysis of the results and how many could not, for various reasons, be so used.

Table 1

	Type of Case					
	Control	Rubella	Measles	Chicken-pox	Mumps	Polio-myelitis
Cases registered	6,619	654	139	353	565	34
Cases included in analysis ..	5,717	578	103	298	501	33
Cases rejected:—						
Later found inapplicable to the Enquiry*	269	9	23	16	20	0
Follow-up examinations not completed:—						
Moved to unknown address	233	23	5	17	17	0
Moved overseas	98	14	2	2	12	0
Refused examination	211	23	6	15	12	1
Twins	91	7	0	5	3	0

* Includes cases found to be registered after birth of baby, not pregnant, not born on 31st day of months (controls), incorrect diagnosis (virus series), therapeutic abortions, illegitimate pregnancies, cases with more than one virus infection.

There was a rubella epidemic in Great Britain in 1952 and 458 of the total 654 rubella cases were selected between February and November that year.

In the 578 rubella cases finally available for analysis the stage in pregnancy when infection occurred was:

in 202 cases before the 12th week, 35 per cent.

in 276 cases between the 13th and 28th week, 48 per cent.

in 96 cases between the 29th and 40th week, 17 per cent.

in 4 cases the date of onset was not stated

or

in 4-weekly periods the distribution was:

35 per cent	{	9 per cent	had rubella up to 4th week of pregnancy
		12 per cent	„ „ from 5th to 8th week of pregnancy
		14 per cent	„ „ 9th to 12th week of pregnancy
48 per cent	{	13 per cent	„ „ 13th to 16th week of pregnancy
		14 per cent	„ „ 17th to 20th week of pregnancy
		12 per cent	„ „ 21st to 24th week of pregnancy
17 per cent	{	9 per cent	„ „ 25th to 28th week of pregnancy
		9 per cent	„ „ 29th to 32nd week of pregnancy
		5 per cent	„ „ 32nd to 36th week of pregnancy
		3 per cent	„ „ 37th to 40th week of pregnancy

The stage in pregnancy at which the other virus infections occurred is shown below:

Table 2

Time in Pregnancy	Measles		Chickenpox		Mumps		Poliomyelitis	
	No.	Percent-age	No.	Percent-age	No.	Percent-age	No.	Percent-age
0-12 weeks ..	37	36	76	25	119	24	9	27
13-28 weeks ..	46	45	144	50	231	47	24	73
29-40 weeks ..	20	19	77	25	147	29	0	—
Not stated ..	0	—	1	—	4	—	0	—
	103	—	298	—	501	—	33	—

During the latter part of 1950 and the beginning of 1951 there was a national epidemic of virus influenza. This was particularly severe in Liverpool and Manchester. Over a period of eight weeks the opportunity was taken to include in this enquiry cases of influenza occurring during pregnancy. The Medical Officers of Health in these two cities selected and followed up any such cases which came to their notice in the authorities' ante-natal clinics. If the diagnosis was not confirmed by a doctor only those cases in which the patient had been confined to bed for more than 24 hours with "influenza" were accepted as influenza cases. One hundred and sixty eight cases were registered as influenza; 42 (25 per cent) occurred within the first 12 weeks, 101 (60 per cent) occurred between the 13th and 28th weeks and 25 (15 per cent) occurred between the 29th and 40th weeks of pregnancy. In two cases the week of onset was not stated.

Tables A-D* show that the cases in the enquiry comprise a representative sample of pregnant women. The age and parity distributions are similar in the control and virus groups and in the country as a whole. The institutional confinement rate, 65 per cent in the control group and 64 per cent in the rubella group, corresponds with the national rate of 64.3 per cent: the other virus groups correspond reasonably well except poliomyelitis where, as might be expected, a higher proportion of births, 85 per cent, were in hospitals. The geographical distribution of cases in the virus and control groups is, on the whole, similar. The proportion of multiple births—twins—is similar in both groups and corresponds with the generally expected rate. Twin pregnancies were not included in the main analysis of results.

The record cards have been analysed to show how the outcome of the pregnancies complicated by each of the virus diseases compares with that of the control series in which no such infections occurred, the items compared being abortions, still births, infant deaths and congenitally malformed children. The duration of the period of observation of each case varied according to the date of selection. Control cases were selected on the mother's first visit to her doctor or midwife, usually in the early months of pregnancy, whereas virus cases might be selected early or late in pregnancy following the occurrence of the infection. Actually, as shown in Table F, 83 per cent of control cases, compared with 65 per cent of rubella cases, and between 52 per cent and 76 per cent of the other

* The lettered Tables are those in Appendix 1 pages 75 to 97.

virus groups were selected up to the 28th week of pregnancy. The period of observation had a bearing on the risks of miscarriage and premature termination of pregnancy; the closer the date of selection to the 28th week of pregnancy the smaller the chance of miscarrying, and after the 28th week the chance would be nil; the closer the date of selection to full time the smaller the chance of premature delivery, with attendant risks to the infant. So, any estimation or comparison of the hazards of pregnancy should take account of the period during which the pregnancy was under observation. This has been done in the analysis.

III. END RESULTS OF THE PREGNANCIES UNDER OBSERVATION

Pregnancies complicated by each of the virus infections have been compared with those of the control group in respect of abortions, still births, live births, premature births and infant deaths. Twin pregnancies have been excluded from this analysis. Table G is a summary showing how the outcome of pregnancies complicated by each of the virus infections compares with the outcome which the control series would lead one to expect. The figures for the "expected" outcome have been calculated from the accumulated experience of all control cases selected earlier than the dates of selection of the cases in the respective virus groups, and in which the pregnancy had not already ended. The calculation was made in such a way that the proportions selected at each stage of pregnancy were the same as in the respective virus infection group—i.e. the controls were standardized for the period of risk.

The outcome of the 5,717 pregnancies in the control series is shown below:

Table 3

Control Preg- nancies	Abortions		Still Births		Live births		Infant Deaths				Children alive at 2 years		Premature births, 5½ lb. or less (live and still)	
	No.	%	No.	%	No.	%	1st Year	2nd Year	Total No.	%	No.	%	No.	%
5,717	92	1.6	156	2.7	5,469	95.7	141	11	152	2.7	5,317	93.0	385	6.4

Enquiries were made about all pregnancies reported to have ended in abortion. Therapeutic abortions have been excluded from this investigation and the analysis includes only those which were apparently spontaneous. In the control series there were four therapeutic abortions, two because of toxæmia of pregnancy and two for reasons not stated. Amongst the virus series six therapeutic abortions were undertaken, all in the rubella group.

A broad comparison with the national rates for the years concerned shows that the control series provides a fairly representative sample of the sequence of pregnancy, childbirth and infant mortality. The comparison is necessarily rough because twins and illegitimate births are excluded from the control figures.

Table 4

	Still birth rate per 1,000 total live and still births	Infant mortality rate per 1,000 live births	Neonatal mortality rate per 1,000 live births	Premature births 5½ lb. or less per cent all births
National rates { 1950	22.7	29.6	18.5	
1951	23.0	29.7	18.8	
1952	22.7	27.6	18.3	7.0
1953	22.5	26.8	17.7	7.5
Control series 1950-1953 ..	27.7	25.8	15.4	6.8

COMPARISON OF RESULTS OF RUBELLA AND CONTROL PREGNANCIES

The pregnancies complicated with rubella differed from those of the control pregnancies by yielding considerably more pre-natal and infant deaths. The percentage of abortions in the rubella pregnancies was 1.9 compared with 1.2 amongst the controls; of still births from these pregnancies 3.5 compared with 2.5; of live births 94.6 compared with 96.3; of deaths before 2 years of age 4.2 compared with 2.5; and of children alive as the outcome of these pregnancies at two years 90.4 compared with 93.8.

Division of rubella pregnancies into three groups according to the stage in pregnancy when infection occurred, i.e. up to the 12th week, between the 13th and 28th week and between the 29th and 40th week, shows that the higher mortality was almost entirely limited to those in which infection was within the first 12 weeks. There were 202 cases of rubella infection within the first 12 weeks of pregnancy. Abortion occurred in ten cases, 5.0 per cent compared with an expected 2.4 per cent. Still birth occurred in nine cases, 4.5 per cent compared with an expected 2.4 per cent; (the still birth rate was doubled when infection occurred within the first four weeks and trebled when it was between the 5th and 8th week). Live births, 183, were consequently fewer, 91 per cent compared with 95 per cent. There were 14 infant deaths before the age of two, 6.9 per cent compared with 2.4 per cent and 169 children alive at two years, 84 per cent compared with an expected 93 per cent. These variations of the outcome of various groups of pregnancies are set out in the table below:

Table 5

Type of case	Percentage of abortions	Percentage of still births	Percentage of live births	Percentage of deaths before two years	Percentage of children alive at two years
Rubella in first 12 weeks	5.0	4.5	90.5	6.9	83.6
Control (standardised)	2.4	2.4	95.2	2.4	92.8
Rubella at 13th week and over	0.3	3.0	96.7	2.7	94.0
Control (standardised)	0.5	2.6	96.9	2.6	94.3

Abortions

There were 11 apparently spontaneous abortions in the rubella series and Table G shows that the abortion rate was higher in the 202 pregnancies complicated by rubella within the first 12 weeks, than in the control cases under observation from the same time, 5.0 per cent compared with 2.4 per cent. A doctor had confirmed the diagnosis of rubella infection in eight cases as either mild or moderate, and in one case as "fairly severe".

The cause of abortion was given in only one case, that of a third pregnancy of a woman with Rh-negative blood.

Although therapeutic abortions have been excluded from the analysis of the results of this enquiry it is worth recording that six pregnancies complicated with rubella in the first ten weeks of pregnancy were so terminated for that reason. Only in two cases has any information been given about the products of abortions. One pregnancy, complicated with rubella in the 10th week, was terminated

in the 27th week and nothing abnormal was observed in the foetus. The other pregnancy was terminated at the 13th week because of rubella between the 5th and 7th weeks and the fact that this mother already had one child who was blind. The foetus showed no signs of abnormality and the eyes, on histological examination, were found to be normal.

Still births

There were 20 still births in the rubella series of 578 cases. This was a higher proportion than in the control series, 3.5 per cent as compared with 2.5 per cent. Table 6 gives particulars of these still births.

Table 6. Twenty Rubella Still births

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when rubella occurred			Gestation period in weeks	Birth weight lb. oz.	Suggested cause or condition of still birth
			0-12th	13th-26th	27th-40th			
6240	21	0	1 ⁺⁺⁺			40	2 11	No abnormality
6205	21	0	3 ⁺⁺⁺			41	4 6	Macerated
6386	26	0	3 ⁺⁺⁺			40	not stated	Congenital heart disease
3979	35	4	5 ⁺⁺⁺			40	not stated	Not known
6190	22	1	5 ⁺⁺⁺			31	not stated	A domestic upset
6358	23	0	5			37	3 0	Not known
6063	27	2	7 ⁺⁺⁺			35	2 8½	Not known. Macerated
6402	26	2	7 ⁺⁺⁺			38	3 3	Macerated
6171	25	0	8 ⁺⁺⁺			32	not stated	Macerated
6426	33	3		14 ⁺⁺⁺		37	8 0	Macerated
6456	32	1		15 ⁺⁺⁺		42	8 0	Breech delivery, arms extended. Asphyxia neonatorum
6316	17	0		18 ⁺		46	8 9	Prolapsed cord. No abnormality
6086	28	0		20 ⁺⁺⁺		39	7 13	Idiocycele
6406	20	0		22 ⁺⁺⁺		40	6 0	Large meningocele
6089	23	3		26 ⁺⁺⁺		38	9 4	Macerated
6118	29	1		28 ⁺⁺⁺		40	6 0	Severe accidental haemorrhage
6413	25	4			29 ⁺⁺⁺	33	3 12	(Previous pregnancies—two miscarriages and one still birth)
5903	28	1			31 ⁺⁺⁺	34	5 0	Macerated. Three heavy falls during pregnancy
6258	41	0			32 ⁺⁺⁺	36	4 12	Macerated
6293	35	3			37 ⁺⁺⁺	40	6 9	Anencephaly, cleft palate and hare lip

⁺=infection confirmed by doctor. ⁺⁺=infection mild. ⁺⁺⁺=infection moderate. ⁺⁺⁺⁺=infection severe

Three still births, 0.5 per cent of all rubella pregnancies compared with 0.8 per cent of all control pregnancies, were due to obstetric complications. The

mother of another still birth had suffered two previous miscarriages and a still birth. In these four cases the rubella infection occurred between the 15th and 29th weeks of pregnancy and the infants showed no congenital malformations. In nine of the remaining 16 still births, rubella infection occurred within the first 12 weeks of pregnancy. Of the 202 cases of rubella in the first 12 weeks of pregnancy the percentage of still births was 4.5.

Major congenital malformations, distinguished in the tables by italics, were present in four of the 20 still births, 20 per cent compared with 18 per cent in the control still births. The incidence of particular malformations differed in the rubella and control still births. Congenital heart disease of which there was one case (rubella at 3rd week), did not occur at all amongst the controls; meningocele occurred twice, 10 per cent, (rubella in 20th and 22nd weeks) and five times in the controls, three per cent. There was one case of anencephaly, five per cent, (rubella in 37th week) compared with 12 cases in the controls, eight per cent. The association of anencephaly with cleft palate and hare lip in a rubella still birth did not occur at all amongst the controls. No conclusions can be drawn from these variations because of the small number of rubella still births and the incomplete information given about many of the still births, both rubella and control.

Twenty-four children of the 578 mothers who had rubella during pregnancy died before two years of age. All the deaths occurred during the first year of life, representing an Infant Mortality Rate of 43.9 per 1,000 live births. Of 202 mothers who had rubella during the first 12 weeks of pregnancy 183 had live-born children, 14 of whom died within the first year of life, representing an infant mortality rate for this group of 76.5. This accounted for more than half of all the infant deaths in the rubella series. In the control series of 5,469 live-born children 152 died before 2 years of age: 93 per cent of these died in the first year of life giving an Infant Mortality Rate of 25.8. The national rates for the years under review were between 29.7 and 26.8.

Table 9 gives details of the "rubella" infant deaths. Comparison with the infant deaths in the control series shows some similarities and some variations. There was little difference in the proportion of deaths at various ages; 50 per cent of rubella deaths and 41 per cent of control deaths occurred within the first week of life. Forty-six per cent of rubella infants who died and 39 per cent of controls weighed 5½ lbs. or less at birth. Respiratory infections and malformations were the main causes of death.

Table 7. Causes of Death

	Rubella Group		Control Group	
		%		%
Respiratory infection alone	9	17	40	26
Respiratory infection plus congenital malformations..	5	21	8	5
Congenital malformations	6	25	39	26
Prematurity	1	4	21	14
Atelectasis	2	8	10	6
Purpura fulminans	1	4	—	—
Other Causes	—	—	34	22

Major congenital malformations were observed in 11, i.e. 46 per cent of the rubella infants who died and in 47, i.e. 34 per cent of the controls. The incidence of particular malformations in these two groups of infants is compared below:

Table 8.

	24 Rubella Deaths		152 Control Deaths	
	Number	%	Number	%
Congenital heart disease alone or in association with other malformations (rubella, 3, 3, 4, 5, 12 wk.)	5	20.8	14	9.2
Atresia of intestine or alimentary tract (rubella 5, 15 wk.)	2	8.3	1	0.7
Cleft palate (rubella 6 wk.)	1	4.2	3	2.0
Pyloric stenosis (rubella 22 wk.)	1	4.2	2	1.3
Spina bifida (rubella 19 wk.)	1	4.2	10	6.6
Enlarged liver (rubella 21 wk.)	1	4.2	nil	
Cataract (rubella 5, 4 wk.)	2	8.3	nil	

Further consideration is given to these malformations in Chapter IV.

Table H compares the still birth and death rates in mature infants (those born after the 36th week of pregnancy) in the control and rubella series. Both still birth and death rates of infants with major malformations in the rubella series correspond closely with those in the controls, but amongst infants without recorded major malformation whose mothers contracted rubella in the first 12 weeks of pregnancy 3.3 per cent were still born and 3.3 per cent died under 2 years, compared with 1.3 per cent and 1.4 per cent respectively in the control series.

Live births and surviving children

Pregnancies complicated during the first 12 weeks by rubella ended more often in abortion and still birth than did the control pregnancies so there were fewer live born infants—and the higher death rate of these rubella infants further reduced the proportion of pregnancies from which there were children alive at two years of age. Of 100 complicated pregnancies there were 91 live-born infants, seven of whom died leaving 84 alive at two years. The comparative numbers for 100 control pregnancies were 95 live born infants, two infant deaths and 93 surviving infants. (Figure 1 page 22).

Table 9. Twenty-four

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when rubella occurred			Gestation period in weeks	Birth weight lb. oz.	Age	
			0-12th	13th-28th	29th-40th			Within 24 hours	2nd-7th day
5909	25	5	5 ^m			38	4 0		
5999	26	1		15 ^m		40	7 0		4
5925	23	0	7 ^m			38	7 15		3
5933	43	3	10 ^m			34	5 12		2
5978	24	0		15 ^m		36	4 10		5
5991	19	0			36 ^m	38	3 11		2
5992	20	0	12 ^m			41	7 14		
5995	23	1		19		39	5 12		
6026	28	1	5 ^m			41	4 4		4
6039	22	0	4 ^m			41	4 15	2 hours	
6055	30	1		22		35	4 5		
6083	22	1	3			38	5 4		3
6100	24	0	4 ^m			41	5 5		
6110	18	0	3 ^m			40	5 8		
6132	25	2	12 ^m			39	4 8		3
6193	29	3		21 ^m		40	6 0		
6253	24	0	6 ^m			41	4 7		
6301	17	0		23		42	6 0		
6309	29	0		21 ^m		43	7 3	10 minutes	
6355	26	2	5 ^m			42	6 8		6
6377	37	5		28 ^m		43	10 0		
6427	32	1	9 ^m			33	Not known	22 hours	
6449	30	1	10 ^m			43	6 11		
6451	25	0		19 ^m		42	9 1		

* = infection confirmed by doctor

^m = infection mild

Rubella Infant Deaths

nt death			Cause of death	Other conditions present
8th-30th day	1st-12th month	2nd year		
	8		Pneumonia. <i>Congenital heart disease</i>	<i>Cataract</i>
			Neonatal pneumonia—Post mortem	None
			Pneumonia	None
			Prematurity. (All other pregnancies (3) premature but children lived)	None
			<i>Duodenal atresia. Anomaly of mesenteric blood vessels. Malrotation of gut</i>	None
			Atelectasis due to maternal toxæmia—Post mortem	None
	3		Acute bronchopneumonia	None
	1		<i>Spina bifida</i>	None
			Hæmorrhagic bronchopneumonia—Post mortem	None
			<i>Congenital heart disease. Porencephaly</i>	<i>Cataract</i>
	1		Bronchopneumonia and operation for <i>pyloric stenosis</i> —Post mortem	Enlarged liver and spleen
			<i>Multiple congenital deformities including congenital heart disease</i>	
	2		Bronchopneumonia	Deformity of forehead, crano-stenosis of frontal bone
	8		Bronchopneumonia and <i>congenital heart disease</i>	None
			<i>Congenital heart disease</i>	None
	5		Purpura fulminans—Post mortem	None
	3		Bronchopneumonia	<i>Defect in soft palate—cleft</i>
	6		Bronchopneumonia	None
			Intrapartum asphyxia following caesarean section for foetal distress. Post mortem— <i>large cystic swelling—? hæmangioma, liver</i>	None
			Pneumonia associated with <i>atresia of oesophagus</i>	None
	2		Capillary bronchitis	None
			Atelectasis	None
	1		Bronchopneumonia	None
	2		Toxæmia and pneumonia	None

^M—infection moderate

^S—infection severe

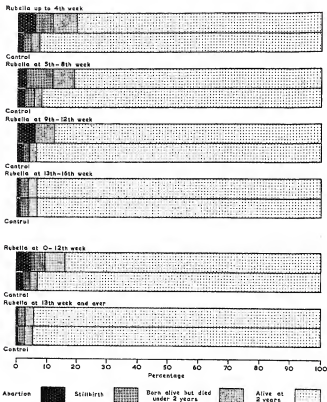


Fig. 1. Survival of the infant in pregnancies complicated by rubella, (according to the stage when rubella occurred), and in control pregnancies (standardized for period under observation).

Prematurity

Table 10 compares the *length of gestation* of rubella pregnancies with a standardized control group. The proportion of premature births, defined as cases of 29 to 36 weeks' gestation was 4.7 per cent in the rubella group, compared with 4.4 per cent expected from the controls. There was, however, a suggestion of a higher proportion of such premature births when rubella had occurred in the first 12 weeks of pregnancy.

Table 10. Comparison of gestation periods of rubella and control pregnancies

Week of onset of Rubella	No. of cases	Week in which delivered										
		Up to 28th week		29th to 32nd weeks		33rd to 36th weeks		Total 29th to 36th weeks		After 36th week		
		No.	%	No.	%	No.	%	No.	%	No.	%	
Up to 12th week ..	202	Actual	10	5.0	2	1.0	11	5.4	13	6.4	179	88.6
		Expected	2.4	1.2	3.2	1.6	6.4	3.2	9.6	4.8	190	94.0
13th to 28th weeks	276	Actual	1	0.4	0	—	9	3.3	9	3.3	266	96.3
		Expected	1.4	0.5	3.2	1.2	9.4	3.4	12.6	4.6	262	94.9
After 28th week ..	96	Actual	—	—	0	—	5	5.2	5	5.2	91	94.8
		Expected	—	—	0.4	0.6	2.4	2.5	2.8	2.9	93.2	97.1
All stages	574	Actual	11	1.9	2	0.3	25	4.4	27	4.7	536	93.4
		Expected	3.8	0.7	6.8	1.2	18.2	3.2	25.0	4.4	515.2	94.9

Table K1 shows the proportion of infants delivered after the 36th week of pregnancy who were *premature by birth weight*. In the control group 4.3 per cent and in the rubella group 8.8 per cent weighed 5½ lb. or less. The excess of small infants occurred when rubella had been within the first 12 weeks of pregnancy; the percentage then was 17.7, whereas in all other rubella cases it was 4.1, which was similar to the controls. Also the death rate of premature infants during the first two years of life was highest in the group whose mothers had rubella within the first twelve weeks of pregnancy, 29 per cent compared with 7 per cent when rubella had occurred later in pregnancy and 11 per cent in control premature infants. The highest proportion of premature infants was found amongst the malformed infants who died and whose mothers had rubella during the first 12 weeks of pregnancy.

A better comparison of birth weights in the rubella and control groups can be obtained by comparing cases delivered after similar gestation periods. Table K2 shows the median birth weights of live born infants delivered at the 39th to 42nd weeks of pregnancy. This shows that, where the mother had rubella in the first 12 weeks of pregnancy, the median birth weight of infants born at full term was 7 lb. 1 oz. and that they were generally lighter than either the control infants, with a median of 7 lb. 6 oz. or those whose mothers had rubella later than the 12th week, whose median birth weight was 7 lb. 8 oz.

Tables K3 and K4 show the distribution of the weights of live born infants in the control and rubella series who were born after 39 to 42 weeks' gestation. Table K3 shows that infants whose mothers had rubella up to the 12th week of pregnancy had a lower range of birth weights at each week of delivery than the controls. Only 1 per cent of the control infants born at the 39th week weighed between 4 and 5 pounds, whereas 12 per cent of the rubella infants fell into this group. At the 42nd week only 0.1 per cent of the controls weighed between 4 and 5 pounds, compared with 6 per cent in the rubella series. At the other end of the range between 4 per cent and 14 per cent of the controls weighed over 9 lb. compared with 0 per cent up to 6 per cent in the rubella series. Table K4 shows that most of the deficiency in birth weight occurred in the malformed infants whose mothers had rubella in the first 12 weeks of pregnancy.

COMPARISON OF RESULTS OF MEASLES AND CONTROL PREGNANCIES

One hundred and three pregnancies were reported as being complicated by measles. Table G shows that the proportions of abortions and still births differed little from those in the control series but the infant death rate was higher and fewer infants survived to 2 years of age. The increase in deaths occurred amongst the 37 infants whose mothers had measles in the first 12 weeks of pregnancy, six of whom died. There were only 2 infant deaths from the 66 pregnancies in which infection occurred after the 12th week.

A simple percentage comparison of the outcome of the measles and the control pregnancies is shown below:

Table 11.

	Abortions	Still births	Live-born infants	Infant deaths under 2 years	Infants alive at 2 years
All measles pregnancies	1.9	1.9	96.2	7.8	88.4
Controls	1.0	2.7	96.3	2.3	94.0
Measles within first 12 weeks	2.7	2.7	94.6	16.2	78.4
Controls	1.9	2.7	95.4	2.4	93.0

Details of the still births and infant deaths are given in Tables 13 and 14.

The proportion of dead infants with major malformations was higher, 50 per cent, than in the control series, 34 per cent: the death rate of infants with major malformations was also higher 50 per cent compared with 29.1 per cent. The malformations were varied but it is noteworthy that one child had the combination of cardiac and eye defects which is observed so often in "rubella" children. In this case measles infection was in the 35th week of pregnancy.

The malformations are considered in a later chapter.

COMPARISON OF RESULTS OF CHICKENPOX AND CONTROL PREGNANCIES

The 298 pregnancies complicated by chickenpox did not vary in outcome from the control pregnancies. Percentage comparison was as follows:—

Table 12.

	Abortions	Still births	Live births	Infant deaths under 2 yrs.	Alive at 2 yrs.
Chickenpox ..	1.3	1.7	97.0	2.7	94.3
Controls	0.8	2.6	96.6	2.5	94.1

Particulars of still births and infant deaths are given in Tables 15 and 16.

In three of the five still births maternal infection was within the first 12 weeks of pregnancy but other causes are suggested in three cases. Only one still birth had showed a congenital abnormality, hydrocephaly,—infection was in the 23rd week of pregnancy.

Amongst the children who died were three malformed; each had a congenital heart defect, but this incidence was no greater than that found in the control series. Maternal infection was between the 22nd and 34th weeks of pregnancy.

Table 13. Two Measles Still Births

Case No.	Mother's age	Week in pregnancy when measles occurred			Gestation period in weeks	Birth weight lb. oz.	Suggested cause or condition of still birth
		0-12th	13th-28th	29th-40th			
6957	28	3	6		39	1 15½	Macerated. No obvious defects but measles said to be cause. (Mother had two previous live births and a miscarriage).
6934	21	1	25		36	2 8	Anencephalic monster. Breech delivery, extended arms and legs. Previous pregnancy ended in miscarriage

Table 14. Eight Measles Infant Deaths

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when measles occurred		Gestation period in weeks	Birth weight lb. oz.	Age at death					Cause	
			0-12th	13th-40th			Within 24 hours	2nd-7th day	8th-30th day	1st-12th month	2nd year		
6924	27	2	4 ^{am}		30	2 11	11½ hrs		18			13 mths	Congenital atelectasis and prematurity Pneumonia due to cerebral injury (face presentation) Cause not known. <i>Dextrocardia</i> Bronchopneumonia Bronchopneumonia, Epilepsy, <i>Hydrocephalus</i> 1. Bronchopneumonia, 2. Atelectasis, 3. <i>Hemiatrophy of cerebellum</i> . At birth: difficulty in sucking—? cerebral abnormality 1. <i>Congenital heart disease</i> , 2. Otitis media. At birth: bilateral talipes, <i>bilateral corneal opacities</i> , loud systolic murmur Cerebral haemorrhage due to torn tentorium
6920	28	2	6 ^s		44	6 4							
6955	27	1	6 ^{as}		41	7 5		7			2	2	
6917	22	1	10 ^c		39	4 12							
6961	24	3	10 ^{am}		40	9 3							
6987	21	0	3 ^{am}		40	4 11							
6968	27	2		35 ^{ab}	40	6 14					11		
6925	18	0		37 ^{am}	40	5 8		6					

* = infection confirmed by doctor.

m = infection mild.

M = infection moderate.

s = infection severe.

Table 15. Five Chickenpox Still births

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when chickenpox occurred		Gestation period in weeks	Birth weight lb. oz.	Suggested cause or condition of still birth
			0-12th	13th-28th			
7349	31	1	6 ^M		40	6 12	Nil on post mortem. Cause unknown but possibly due to mild pre-eclampsia. No abnormality of macerated foetus. Syphilis in mother. Asphyxia. <i>Hydrocephalus</i> .
7323	30	2	6		42	Not stated	
7206	27	0		25 ^M	39	Not stated	
7127	19	0	12 ^M		41	9 2	
7174	23	4		23	33	Not stated	

Table 16. Eight Chickenpox Deaths

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when chickenpox occurred		Gestation period in weeks	Birth weight lb. oz.	Age at death					Cause	
			0-12th	13th-28th			29th-40th	Within 24 hours	2nd-7th day	8th-30th day	1st-12th month		2nd year
7051	25	1	1 st		40	7 6		1			14 mths	Pneumonia, atelectasis.	
7184	20	0	8 th		39	7 0						Tuberculous meningitis.	
7145	28	1		37 th	37	6 12			28			Bronchopneumonia, chickenpox. Web toes, both feet.	
7061	27	2		17 th	24	1 1	12 hours					Placenta praevia and prematurity.	
7256	21	1		26 th	41	5 14				7		Bronchopneumonia, congenital heart disease.	
7203	33	2		22 th	44	7 1				2		Congenital heart disease.	
7254	26	2		34 th	42	8 1				6		Syncope. Gross congenital abnormality, heart.	
7179	20	0		17 th	31	3 12				2		Bronchopneumonia, prematurity. At birth: treated for haemorrhagic disease.	

* = infection confirmed by doctor.

M = infection mild.

M = infection moderate.

S = infection severe.

COMPARISON OF RESULTS OF MUMPS AND CONTROL PREGNANCIES

The proportion of abortions, still births, and infant deaths from the 501 pregnancies complicated by mumps at all stages in pregnancy was much the same as in the control series, as shown in Table G and in the simple percentage comparison below:

Table 17

	Abortions	Still births	Live births	Infant deaths under 2 years	Alive at 2 years
Mumps	1.0	1.8	97.2	2.4	94.8
Controls	0.8	2.6	96.6	2.5	94.1

Tables 18 and 19 give particulars of the still births and infant deaths.

The still births show nothing unusual. Two had major malformations, 22 per cent compared with 18 per cent of control still births.

Congenital abnormalities were present in 5 of the 12 children who died, 41.7 per cent compared with 34 per cent of controls: maternal infection was between the 20th and 34th weeks.

The malformations are considered in a later chapter.

Table 18. Nine Mumps Still births

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when mumps occurred			Gestation period in weeks	Birth weight lb. oz.	Suggested cause or condition of still birth
			0-12th	13th-28th	29th-40th			
7850	23	0		20 ^m		41	7 4	<i>Ectopia vesicae and eventration due to failure of fusion of abdominal wall.</i>
7533	28	3		21 ^m		34	2 12	<i>Anencephaly and spina bifida.</i>
7832	31	0		21 ^m		38	4 14	Macerated. Placental insufficiency.
7825	36	2		28 ^m		41	Not stated	Extended breech delivery.
7772	38	3		13 ^m		41	Not stated	Extended breech, premature inspiration.
7717	40	4			38 ^m	41	8 8	No apparent cause but high temperature of mother during attack of mumps which occurred a few weeks before birth may have caused or contributed to death in utero.
7613	20	0		19 ^m		29	5 0	Macerated foetus.
7492	28	1	8 ^m			38	4 12	Macerated.
7422	35	2	5 ^m			42	9 8	Foetal distress in labour.

^m=infection confirmed by doctor. ^m=infection mild. ^m=infection moderate. ^m=infection severe.

Table 19. Twelve Mumps Deaths

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when mumps occurred			Gestation period in weeks	Birth weight lb. oz.	Age at death				Cause	
			0-12th	13th-28th	29th-40th			Within 24 hours	2nd-7th day	8th-30th day	1st-12th month		2nd year
505	22	2			34 ^{mm}	37	3 6				3		Congenital heart disease—Fallot's tetralogy, "Clubhand".
612	22	1		25		41	6 12			20			Congenital occipital meningocele.
573	36	2		20 ^{mm}		41	6 12				6		Congenital heart disease.
405	24	1			29 ^{mm}	41	6 2				6		Congenital heart disease.
776	22	0		22 ^{mm}		46	8 0	24 hours					Asphyxia neonatorum. Mild hydrocephalus, talipes, hypospadias.
407	30	3		18 ^{mm}		41	9 8				11		Fulminating pneumonia.
501	24	1		23		43	8 8				3		Suffocation from inhalation of vomit.
600	36	1		27 ^{mm}		39	5 4		3				Prematurity, asphyxia. (Maternal eclampsia).
654	31	3		23 ^{mm}		36	6 3		2				Neonatal asphyxia. Tentorial tears.
708	26	0			39 ^{mm}	45	10 0	14 hours					Cerebral haemorrhage secondary to forceps delivery. Postmaturity. No congenital disease.
781	34	4	12 ^c			40	6 4						Bronchial pneumonia.
855	31	2			34 ^{mm}	41	8 0		6			14 mths	Bronchopneumonia.

^z—infection confirmed by doctor. ^{mm}—infection mild. ^{mm}—infection moderate. ^{mm}—infection severe.

POLIOMYELITIS

Thirty three pregnancies complicated with poliomyelitis were reported and in all of them the infection was within the first 24 weeks. The number is too small for satisfactory comparison with the control pregnancies.

An unusual sequence of fatalities appeared in the six pregnancies in which poliomyelitis occurred between the 9th and 12th weeks: one aborted, two ended in still birth and one of the three live born children died at 7 days of "internal hydrocephaly and spina bifida". In other words in only two of these 6 cases did children survive up to 2 years.

The one abortion occurred at the 16th week following severe poliomyelitis infection at the 9th week. The mother eventually died from poliomyelitis some 5 months later.

Particulars of the two still births and 2 infant deaths are given in Tables 21 and 22.

COMPARISONS OF RESULTS OF INFLUENZA AND CONTROL PREGNANCIES

One hundred and sixty six affected pregnancies were reported: in 99, more than half, infection was between the 13th and 28th week. The results do not differ very much from the controls and are shown in Table G and more simply below:

Table 20

	Abortions	Still births	Live births	Infant deaths under 2 years	Alive at 2 years
Influenza	0.6	1.2	98.2	3.6	94.6
Controls	1.0	2.7	96.3	2.5	93.8

There were six infant deaths, and five of these were cases in which the maternal infection was between the 20th and 27th weeks, but particulars of the causes of these deaths showed nothing unusual. Malformations were present in one of the children who died and in one of the two still births. (Tables 23 and 24).

Table 21. Two Poliomyelitis Still births

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when poliomyelitis occurred			Gestation period in weeks	Birth weight lb. oz.	Suggested cause or condition of still birth
			0-12th	13th-28th	29th-40th			
7983	29	4	9 ^{AM}			32	3 8	Combined accidental haemorrhage.
7966	36	2	12 ^{AM} paralytic			36	2 4	Macerated. Patient had a severe toxæmia for at least nine weeks prior to delivery. Rhesus negative but no antibodies at time of delivery.

Table 22. Two Poliomyelitis Deaths

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when poliomyelitis occurred			Gestation period in weeks	Birth weight lb. oz.	Age at death				Cause	
			0-12th	13th-28th	29th-40th			Within 24 hours	2nd-7th day	8th-30th day	1st-12th month		2nd year
7970	21	0	12 ^{AM}			35	4 12		7				<i>Hydrocephalus. Large spina bifida. Bilateral talipes.</i>
7972	23	0		24 ^x		39	4 6	8½ hours					<i>Atelectasis, prematurity.</i>

^x—infection confirmed by doctor.^m—infection mild.^M—infection moderate.^S—infection severe.

Table 23. Two Influenza Still births

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when influenza occurred			Gestation period in weeks	Birth weight lb. oz.	Suggested cause or condition of still birth
			0-12th	13th-28th	29th-40th			
8117	41	4		15 ^m		39	7 0	Macerated, but no abnormalities.
8058	24	0		23 ^s		44	7 0	Hydrocephalus, macerated. Cause unknown.

Table 24. Six Influenza Deaths

Case No.	Mother's age	Previous pregnancies	Week in pregnancy when influenza occurred			Gestation period in weeks	Birth weight lb. oz.	Age at death					Cause
			0-12th	13th-28th	29th-40th			Within 24 hours	2nd-7th day	8th-30th day	1st-12th month	2nd year	
8073	25	0	5 ^s			41	7 3				6		Bronchopneumonia.
8145	27	2		20 ^m		44	8 0				2		Gastroenteritis.
8146	23	2		21 ^m		42	9 0				1		Accidental death—inhalation of vomit.
8083	23	1		26		31	3 4		6				Prematurity, atelectasis.
8134	21	0		26		45	5 12					21 mths	Bronchopneumonia.
8009	25	2		27 ^m		44	6 9				1		(a) Meningitis, (b) Meningococcal hydrocephalus, spina bifida, talipes.

^s=infection confirmed by doctor.^m=infection mild.^m=infection moderate.^s=infection severe.

IV. MAJOR CONGENITAL DEFECTS

All recorded congenital defects in still births and in infants born alive have been divided into two main groups, "Major Defects" and "Minor Defects". The division was arbitrary. The guiding principle was to list as major those defects which might affect the life of the foetus or seriously handicap the living child. Conditions, such as talipes, which in a mild form would cause some inconvenience, but if severe would be a serious handicap, were placed in the "minor" group when there was no indication of their severity. Certain seemingly minor abnormalities which are suggestive of the presence of a more serious condition have been called "suspicious defects". For example, "slow in talking" might be an indication of unrecognised deafness.

Table L compares the occurrence of infants with major defects in the control group and in each virus group, according to the stage of pregnancy in which the infection occurred.

RUBELLA GROUP

The 578 pregnancies complicated with rubella produced 547 live children of whom 37 had major congenital defects. The 5,717 pregnancies in the control series produced 5,469 live born children of whom 128 had major defects. The proportion of children with major defects was greater in the rubella group than in the control group—seven per cent compared with two per cent. Nine of the 37 malformed rubella children had multiple defects, a higher proportion than was recorded amongst the control malformed children.

Table L and Figure 2 show how the occurrence of the defects is related to the stage of pregnancy during which infection took place. When rubella had occurred within the first 12 weeks of pregnancy 29 children were malformed, 15.8 per cent compared with 2.3 per cent in the control group. When rubella occurred between the 13th and the 28th week of pregnancy 7 children, 2.6 per cent, were malformed. When rubella occurred later in pregnancy defects appeared only occasionally.

Table 25 gives particulars of the 37 rubella children with major defects and of 18 others who showed "suspicious defects". The most striking feature is that 14 children had a congenital defect of the heart, associated in six of them with cataract. In all the 14 cases the maternal infection had been within the first 13 weeks of pregnancy.

The incidence of *congenital heart disease* in the rubella children was 2.6 per cent but as all but one of the affected children were born to mothers who had rubella within the first 12 weeks of pregnancy the incidence in that group of 183 children was 7.1 per cent. Seven of the 14 cardiac cases had associated defects: three had cataract alone, three had cataract with, in one case deafness, in another backwardness and in the third porencephaly; one had multiple defects. Congenital malformations of the heart were observed in 26 control children—an incidence of 0.5 per cent and in only four of them were there

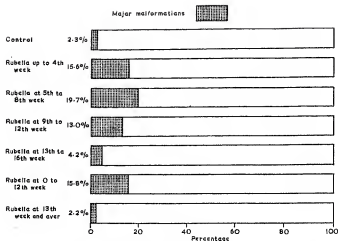


Fig. 2. Incidence of major congenital malformations noted before the age of 2 years in live born infants in the rubella series, (according to the stage of pregnancy when rubella occurred), and in control cases.

associated defects (1) hydrocephalus, (2) congenital nystagmus, (3) hypertelorism and (4) Hirschsprung's disease.

Cataract, the second commonest malformation, occurred in ten children, six of whom had also heart malformations. Maternal rubella in all ten cases was within the first nine weeks of pregnancy. The incidence of cataract in all rubella children was 1.8 per cent and in those whose mothers had rubella within the first 12 weeks of pregnancy it was 5.5 per cent. Amongst the control children two had cataracts (neither child had any other defect) and two, one of whom was also mentally backward, had defective vision. The incidence of eye defects in this group was 0.07.

Deafness was found in five rubella children, one of whom had also a congenital heart malformation and cataract. In all cases rubella had been within the first 12 weeks of pregnancy. The incidence of deafness in all rubella children was 0.9 per cent and when maternal infection was within the first 12 weeks of pregnancy it was 2.7 per cent. Four of the control children were deaf—an incidence of 0.07 per cent. One deaf child had also ptosis and generalised muscular weakness and another had a lymphangioma.

In very young children the presence of deafness, especially if it is unilateral, may not be detected unless special tests are undertaken but it would seem reasonable to suspect conditions such as "general backwardness" or "slowness in talking" as being indications of the possibility of some loss of hearing. In the rubella series deafness was suspected in 6 children and 3 children showed some backwardness. In six of these nine "suspicious" cases, rubella had been in the first 12 weeks of pregnancy. It is therefore possible that the incidence of deafness

Table 25. Major and "Suspicious" Defects in Live Born Children—Rubella Group

Case No.	Week in pregnancy when rubella occurred					Mother's age	Previous pregnancies	Gestation period in weeks	Birth weight lb. oz.	Defects					Dead by 2 yrs.	Alive at 2 yrs.
	0-4th	5th-8th	9th-12th	13th-16th	17th-40th					Mental	Heart	Eye	Ear	Other		
MAJOR DEFECTS																
6034	1st W					27	2	41	5 8	Mentally backward child	C.D.H.	Cataract			1	
6463				15th W		25	4	41	6 8	Backward					1	
6360			10th W			35	2	40	7 0	Mentally backward					1	
6270		6th W				24	0	39	4 4	Very backward					1	
5909		5th W				25	5	38	4 0		C.D.H.	Cataract			1	
6123		5th W				29	0	41	6 5		C.D.H.	Cataract			1	
6447			9th W			20	6	42	5 12		C.D.H.	Cataract			1	
6039	4th W					22	0	41	4 15		C.D.H.	Cataract		Porencephaly	1	
5998			9th W			23	1	41	4 13			Cataract			1	
5932			9th W			33	1	39	5 14	Systolic murmur		Cataract		Retarded development	1	
6166	4th W					27	2	39	6 9			Cataract			1	
6319	4th W					39	2	40	7 4			Cataract			1	
6083	3					22	1	38	5 4		C.D.H.	Cataract		Multiple deformities	1	
6110	3rd W					18	0	40	5 8		C.D.H.	Cataract			1	
6425		7th W				20	1	41	6 11		C.D.H.	Cataract			1	
6152		7th W				26	0	42	7 1		C.D.H.	Cataract			1	
6000		8th W				23	1	42	6 12		C.D.H.	Cataract			1	

(Table continued overleaf)

Table 25. (contd.)

Case No.	Week in pregnancy when rubella occurred					Mother's age	Previous pregnancies	Gestation period in weeks	Birth weight lb. or oz.	Defects					Dead by 2 yrs.	Alive at 2 yrs.
	0-4th	5th-8th	9th-12th	13th-16th	17th-40th					Mental	Heart	Eye	Ear	Other		
6132			12 th			25	2	39	4 8		C.D.H.				1	1
6386				13 th		27	3	40	6 13		C.D.H.			Speech very backward		1
6173		5 th				36	3	41	3 13		C.D.H.					1
5990			9 th			33	1	45	4 8		C.D.H.			Flat feet; spasticity, lower limbs		1
6391		8 th				25	1	40	4 13				Deaf			1
6041		7 th				32	3	38	7 1				Deaf			1
6327			10 th			18	0	37	4 10				Partially deaf			1
6133			13 th			24	1	36	4 11				Slight deafness			1
5995					19	23	1	39	5 12				Partially deaf	Spina bifida		1
6253		6 th				24	0	41	4 7				Claf palate	Claf palate and hare lip		1
6094					17	32	2	41	6 8					Atresia, duodenum and multiple deformities including anomaly of mesenteric blood vessels		1
5978				15 th		24	0	36	4 10 ¹					Atresia, oesophagus		1
6055		5 th				26	2	42	6 8					Atresia, duodenum		1
6011			9 th			22	2	38	6 4					Pyloric stenosis. General condition poor		1
5953		8 th				34	4	42	4 13					Pyloric stenosis		1
6009			10 th			20	0	40	8 0					Enlarged spleen and liver. Pyloric stenosis		1
6055					22	30	1	35	4 5					Imperforate anus		1
6341					29	26	2	35	3 13 ¹					Cystic swelling, liver		1
6309				21 st		29	0	43	7 33					Erythroblastosis		1
6193	4 th					29	4	40	8 5							1

Table 25. (contd.)

Case No.	Week in pregnancy when rubella occurred					Mother's age	Previous pregnancies	Gestation period in weeks	Birth weight lb. oz.	Defects					Dead by 2 yrs.	Alive at 2 yrs.	
	0-4th	5th-8th	9th-12th	13th-16th	17th-40th					Mental	Heart	Eye	Ear	Other			
"SUSPICIOUS DEFECTS"																	
6092					16cm	22	1	41	8 0						? deaf	Anaemia	1
6208		6cm				26	0	40	7 4						? deaf		1
6480		8cm				36	3	40	8 8						? deaf		1
6139			10cm			22	1	39	7 8						? deaf		1
6135			12cm			36	4	42	5 12						? deaf		1
6013				13cm		27	0	41	8 0						? deaf		1
6436			12cm			28	2	40	6 4			Slow in all ways. Intelligence may be sub-normal					1
6302	4cm					21	3	41	4 10							Speech development slow	1
5985					26cm	40	2	39	7 6							Speech development slow	1
6438	3cm					28	3	40	8 0			Murmurs					1
6075		7cm				22	0	42	7 12			Murmurs					1
6170					18cm	21	0	43	5 13			Murmurs					1
5955					26cm	23	1	39	7 0			Murmurs					1
6030					28	33	4	36	4 0			Murmurs					1
5973					34cm	37	2	40	8 0			Murmurs					1
6100	4cm					24	0	41	5 5							Craniospina, frontal bone	1
6420				16cm		24	3	45	6 12							Anaemia	1
6180		6				36	2	41	7 7							Anaemia	1

x = confirmed by doctor m = infection mild M = infection moderate S = infection severe C.D.H. = Congenital disease, heart.

may be higher by 1.6 per cent in all rubella children or by 3.3 per cent in those whose mothers had rubella within first 12 weeks of pregnancy. Nineteen of the control children were backward in talking—0.35 per cent. (See also Chapter V).

Mental Defects of varying degree occurred in four of the rubella children, one of whom had also a congenital heart malformation and cataract. Rubella infection in three cases was within the first 12 weeks of pregnancy, and in the remaining case in the 15th week. The incidence in all rubella children was 0.7 per cent and where infection was within the first 16 weeks, 1.5 per cent. In the control series there were 21 mentally defective children, including 7 mongols, and 1 child with primary amentia—an incidence of 0.4 per cent.

Atresia of the oesophagus or intestine occurred in three children: rubella infection was in the 5th, 9th and 15th week of pregnancy—an incidence of 0.5 per cent in all cases and 1.2 per cent in those in whom rubella had been within the first 16 weeks of pregnancy. Only one case was reported in the control series—incidence 0.02 per cent.

Pyloric Stenosis occurred in three children when rubella was in the 8th, 10th and 22nd week of pregnancy. The incidence was 0.5 per cent. Ten cases in the controls gave an incidence of 0.2 per cent.

Cleft Palate occurred twice, once associated with hare lip—rubella infection was in the 6th and 17th weeks—incidence 0.37 per cent. Nine cases in the controls gave an incidence of 0.16 per cent.

In the rubella children the following malformations occurred in single instances: porencephaly (associated with cataract and a cardiac defect), spina bifida, imperforate anus, cystic swelling of liver, enlargement of liver and spleen (in a child with pyloric stenosis) and erythroblastosis.

In Table 26 the incidence of major defects in the rubella and control children is compared.

Abnormalities recorded as "cardiac murmur" and "anaemia" mean little and in the absence of further information such indefinite reports have not been accepted as firm diagnoses. As they may be an indication of a serious condition a comparison of their occurrence in each group of children has been made although its value is questionable. Cardiac murmurs of various kinds were found in eight rubella children and in 56 control children—incidences of 1.5 per cent and 1 per cent. Anaemia, unspecified, was observed in three of the rubella children and in five of the controls, incidences 0.5 per cent and 0.1 per cent. In the rubella cases the maternal infection occurred at varying times throughout pregnancy.

Major congenital malformations appeared in 11 of the 24 rubella children who died, i.e. in 46 per cent of dead children compared with 34 per cent of dead children in the control series. Only cardiac malformations appeared more than once or twice. There were five cases of cardiac malformations—(rubella within first 12 weeks), an incidence of 21 per cent compared with 10 per cent in the control infant deaths. Cataract, twice associated with a heart malformation in the rubella children, did not appear at all in the control children who died.

Five hundred and twenty-three rubella children were alive at 2 years of age; 497, 95 per cent, were well in that they had no major abnormalities, 26, 5 per cent, had major abnormalities and nine, 1.7 per cent, had symptoms suggestive of a hearing defect. (Table 27).

Table 26. Incidence of Defects

Series	Number of cases	Congenital heart disease		Cataract		Congenital heart disease + cataract		Mental defect		Deafness		Suspended deafness		Pyloric stenosis		Cleft palate		Spina bifida		Atresia of gut		Erythroblastosis		All Major defects	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Control																									
(a) live-born	5,455	26	0.48	2	0.04	0	—	21	0.38	4	0.07	19	0.35	10	0.18	9	0.16	13	0.24	1	0.02	10	0.18	128	2.35
(b) alive at 2 years	5,315	12	0.23	2	0.04	0	—	19	0.36	4	0.08	19	0.36	8	0.15	6	0.11	3	0.06	0	—	4	0.08	81	1.52
All embryos																									
(a) live-born	547	14	2.56	10	1.83	6	1.10	4	0.73	5	0.91	9	1.65	3	0.55	2	0.37	1	0.18	3	0.55	1	0.18	37	6.76
(b) alive at 2 years	523	9	1.72	8	1.53	4	0.76	4	0.76	5	0.96	9	1.72	2	0.38	1	0.19	0	—	1	0.19	1	0.19	26	4.97
Rubella (1-12 weeks)																									
(a) live-born	183	13	7.10	10	5.46	6	3.28	3	1.64	5	2.73	6	3.28	2	1.09	1	0.55	0	—	2	1.09	1	0.55	29	15.85
(b) alive at 2 years	169	8	4.73	8	4.73	4	2.37	3	1.78	5	2.96	6	3.55	2	1.18	0	—	0	—	1	0.59	1	0.59	22	13.02

Table 27. Defective Rubella Children Alive at 2 Years

Number of children	Defects	Week in pregnancy when infection occurred		
		0-12	13-24	25-40
1	Mentally backward Congenital heart disease Cataract	1		
3	Mentally backward	6 10	15	
1	Congenital heart disease Cataract Deaf	9		
2	Congenital heart disease Cataract	5 9		
4	Cataract	4 4 9 9		
4	Congenital heart disease	7 7 8	13	
1	Congenital heart disease Speech backward	5		
1	Cleft palate		17	
1	Atresia, Intestine	9		
2	Pyloric stenosis	8 10		
1	Imperforate anus			29
1	Erythroblastosis	4		
4	Deaf	7 8 10 12		
9	Suspected deafness	4 6 8 10 12 12	13 18	26

Table 28. Major malformations according to severity of rubella infection occurring within first 12 weeks of pregnancy

Type of case and degree of severity of Rubella infection				No. of cases	Infants without major malformation		Infants with major malformation		Not stated	
					No.	%	No.	%	No.	%
Control series				5,611	5,431	96.8	156	2.8	24	0.4
Rubella up to 12th week	{	Mild	95	79	83.2	15	15.8	1	1.0	
		Moderate	65	53	81.5	11	17.0	1	1.5	
		Severe	9	7	77.8	2	22.2	0	—	
		Not stated	23	21	91.3	2	8.7	0	—	
		All degrees of severity	192	160	83.3	30	15.6	2	1.0	

In both the control and rubella series the incidence of defective children increases with increasing parity of the mother. There is also a suggestion of a

higher incidence amongst children of older rather than younger mothers. (Tables M and N).

The diagnosis of rubella was confirmed by a doctor in the majority of cases and the severity of infection was assessed, as "mild" in 269 cases, as "moderate" in 195 cases, and "severe" in 36 cases. No indication of severity was given in 15 cases. Although there is a small increase in the proportion of cases with major defects with increasing severity of the infection when it occurred within the first 12 weeks of pregnancy, the differences are very small and it is doubtful if any significance can be attached to this. (Table 28). There is no doubt that many of the severe types of defect were associated with mild infections.

MEASLES

There were 99 live-born children of 103 mothers who had measles during pregnancy and major malformations were present in seven of them. Table L shows that the incidence of malformed children is higher than in the control series, 7 per cent compared with 2.3 per cent. The increase does not appear to be related to the time in pregnancy when infection occurred. The actual malformations, shown in Table 29 are varied. Malformations of the brain and of the heart occur twice and there are single cases of congenital dislocation of hips, pyloric stenosis, and neoplasm. One of the children with a heart defect had also corneal opacities, an association of defects suggestive of a rubella infection.

Four of the malformed children died before the age of two and the high death rate of children with congenital malformations in the measles group has already been mentioned.

Of the 91 children surviving at two years three had major malformations; (1) congenital dislocation both hips; (2) pyloric stenosis; (3) neoplasm. The proportion of malformed children was 3.3 per cent compared with 1.5 per cent in the corresponding group of control children.

Five children had suspicious symptoms, three were slow in talking and two had vague cardiac conditions.

Despite the rather high proportion of malformed children in this group the numbers are too small and the defects too varied to suggest an association with the maternal measles infection.

CHICKENPOX

Only six of the 288 live-born children of mothers who suffered from chickenpox during pregnancy had major congenital malformations, 2.1 per cent compared with 2.3 per cent in the control series. Table L shows nothing of note in regard to the time of infection during pregnancy. The incidence of various defects in the chickenpox and control live-born children does not vary to any great extent. (Table 30).

Table 29. Major and "Suspicious" Defects in Live-born Children—Mentles Group

Case No.	Week in pregnancy when measles occurred					Mother's age	Previous pregnancies	Gestation period in weeks	Birth weight lb. oz.	Defects				Dead by 2 yrs.	Alive at 2 yrs.
	0-4th	5th-8th	9th-12th	13th-16th	17th-40th					Mental	Heart	Eye	Ear		
MAJOR DEFECTS															
6961			10-12			24	3	40	9 3	Epilepsy					
6967	3rd					21	0	40	4 11					Hydrocephalus	
6977			20-23			27	2	41	7 0					Hemistrophy, cerebellum	
6955		6th				27	1	41	7 5	Dextro-cardia				Congenital dislocation, both hips	
6980		8th				28	2	40	6 12					Pyloric stenosis	
6968			35-38			27	2	40	6 14	C.D.H.	Bilateral ectopic eyelashes			Severe talipes	
6942			25-28			21	1	42	10 1	Systolic murmur				Benign neoplasm, breast and skin	
"SUSPICIOUS" DEFECTS															
6938			32-34			32	1	41	6 4	Slow in speaking					
6959		6th				33	3	41	7 6	Slow to talk					
6901			23			38	2	39	7 8	Cyanosis				Very bow-legged	
6912			14th			21	0	37	7 0	Retarded, no speech					
x—infection confirmed by doctor. m—infection mild. M—infection moderate. S—infection severe. C.D.H.—congenital disease, heart.															

Table 30. Major and "Suspicious" Defects in Live-born Children—Chickenpox Group

Case No.	Week in pregnancy when chickenpox occurred				Mother's age	Previous pregnancies	Gestation period in weeks	Birth weight lb. oz.	Defects				Dead by 2 yrs.	Alive at 2 yrs.	
	0-4th	5th-8th	9th-12th	13th-16th					Mental	Heart	Eye	Ear			Other
MAJOR DEFECTS															
7238		7 ²² W			32	2	40	6 0	Mentally backward					Enlarged liver and spleen	1
7256		26 ²² M			21	1	41	5 14		C.D.H.					1
7283		22 ²² M			32	2	44	7 1		C.D.H.					1
7254		34 ²² M			26	2	42	8 1		C.D.H., Dextrocardia					1
7179		17 ²² M			20	0	31	3 12						Haemorrhagic disease of newborn	1
7239		30 ²² M			25	3	39	7 0						Intestinal obstruction—? congenital stenosis of pelvi-ectal junction	1
"SUSPICIOUS" DEFECTS															
7306		31 ²² M			32	2	41	6 12	Backward in talking						1
7262		15 ²² M			31	3	43	8 11		Apical systolic bruit					1
7191		23 ²² M			27	2	38	7 2		? heart lesion					1
7141		36 ²² M			25	1	41	8 8		Murmur ? defect					1
7073	2 ²² M				23	2	40	6 8		Softened but sound at apex				Slight talipes	1

x—infection confirmed by doctor.

m—infection mild.

M—infection moderate.

B—infection severe.

C.D.H.—Congenital disease, heart.

MUMPS

Table L shows no excess of malformations in the children whose mothers had mumps during pregnancy compared with the control children. Table 31 lists the major and suspicious malformations which were reported.

There were 487 live-born children from 501 pregnancies complicated with mumps. Major congenital malformations were present in 11 of them, 2.3 per cent. The proportion is the same as the 2.3 per cent of malformed children found in the control series and the incidence of particular defects is also similar. Maternal infection was most often in the latter half of pregnancy—in 8 cases it was from the 17th week onwards.

The proportion of live-born children alive at 2 years without malformations was 96.3 compared with 95.9 in the control series.

POLIOMYELITIS

Only one of the 30 children born to mothers who had poliomyelitis in pregnancy showed major malformations. Infection was in the 12th week and the child had hydrocephaly, spina bifida and bilateral talipes. She lived only seven days.

INFLUENZA

Amongst the 163 live-born children of mothers who had influenza during pregnancy six had major defects, 3.7 per cent compared with 2.3 per cent in the control series. The defects shown in Table 32, are varied and maternal infection was between the 13th and 27th weeks of pregnancy.

Table 31. Major and "Suspicious" Defects in Live-born Children—Mumps Group

Case No.	Week in pregnancy when mumps occurred					Mother's age	Previous pregnancies	Gestation period in weeks	Birth weight lb. oz.	Defects					Dead by 2 yrs.	Alive at 2 yrs.
	0-4th	5th-8th	9th-12th	13th-16th	17th-40th					Mental	Heart	Eye	Ear	Other		
MAJOR DEFECTS																
4606					40wk	27	3	40	7 12			Cataract and blindness, right eye			1	1
4612					25	32	1	41	6 12							1
7900					39wk	34	1	42	8 8							1
7776					32wk	32	0	46	8 0							1
7505					34wk	22	2	37	3 6			Fallot's tetralogy				1
7573					30wk	36	2	41	6 12			C.D.H.				1
7465					39wk	34	1	41	6 2			C.D.H.				1
7516					26wk	23	2	41	6 6							1
7539		8wk				22	0	40	8 11							1
7819				15wk		39	2	46	9 0							1
7591			10wk			23	1	42	7 3							1
																1

(Table continued overleaf)

Table 31. (contd.)

Case No.	Week in pregnancy when mumps occurred				Mother's age	Previous pregnancies	Gestation period in weeks	Birth weight lb. oz.	Defects				Dead by 2 yrs.	Alive at 2 yrs.	
	0-4th	5th-8th	9th-12th	13th-16th					17th-40th	Mental	Heart	Eye			Ear
"SUSPICIOUS" DEFECTS															
7405			14 ^x		26	2	43	7 12	Slow in talking					1	1
7435					36	2	40	7 6	Backward in talking					1	1
7438					34	0	40	6 12	Slow in talking and walking					1	1
7412					32	1	40	5 10	Backward in talking					1	1
7531					29	3	41	7 14	General development retarded					1	1
7886			14 ^x		27	3	40	5 12		Murmur				1	1
7755					21	0	40	7 12		Murmur				1	1
7752			9 ^{ms}		33	0	37	6 9		Murmur				1	1
7451					26	0	39	6 8		Murmur				1	1
7418	24 ^{ms}				26	1	42	9 6		Murmur				1	1
7757					25	3	41	7 0		Murmur				1	1
7469			12 ^{ms}		19	0	40	7 0		Cyanosis				1	1

x=infection confirmed by doctor.

m=infection mild.

M=infection moderate.

s=infection severe.

C.D.H.=Congenital disease, heart.

Table 32. Major and "Suspicious" Defects in Live-born Children—Influenza Group

Case No.	Week in pregnancy when influenza occurred				Mother's age	Previous pregnancies	Gestation period in weeks	Birth weight lb. oz.	Defects				Dead by 2 yrs.	Alive at 2 yrs.	
	0-4th	5th-8th	9th-12th	13th-40th					Mental	Heart	Eye	Ear			Other
MAJOR DEFECTS															
8009				27 ^{AM}	25	2	44	6 9						Hydrocephalus, spina bifida and talipes	1
8089				26	28	2	41	8 0						Cleft palate and hare lip	1
8093			13 ^{AM}		41	7	43	7 13						Achondroplasia	1
8007				17 ^{AM}	27	1	38	7 2						Absence of left forearm and hand	1
8132				24 ^{AM}	29	4	41	7 6						Backward mentally	1
8138				19 ^{AM}	37	3	42	7 0						Imperforate vagina	1
"SUSPICIOUS" DEFECTS															
8116				28 ^x	27	2	38	6 12						Delayed speech	1
8076				33	28	1	41	6 4						Backward speech	1

Hydrocephalus, spina bifida and talipes
Cleft palate and hare lip
Achoondroplasia
Absence of left forearm and hand
Imperforate vagina

Delayed speech
Backward speech

V. LATER MEDICAL EXAMINATIONS

In the enquiry so far described covering England, Wales and Scotland the arrangements provided for only a brief medical report of any congenital defects found on examination at birth, at one year and at two years of age. Reports on over six thousand children from many different sources naturally involved some variation in standards. Moreover defects such as mental retardation and deafness might not be apparent by the age of two unless special examinations had been made. It therefore seemed desirable to undertake some kind of check on the results already obtained by examination of the children at a later age and, if practicable, by a standard technique. Two series of further examinations have been made and these are described in Sections I and II of this chapter.

In the first instance a number of rubella and control children were examined by a standard technique. In London and Middlesex there were some 50 children whose mothers had rubella during the first 18 weeks of pregnancy. A similar number of suitably matched children was selected from our control series and during 1956 and 1957 arrangements were made for the children to attend the Province of Natal Centre, where complete paediatric examinations including special hearing tests were carried out. The results are presented in Section I below.

Later, in consequence of these findings 180 children throughout England, Wales and Scotland whose mothers had rubella during the first four months of pregnancy were re-examined and the results are presented in Section II below.

SECTION I

(Contributed by Dr. A. D. M. Jackson and Dr. L. Fisch)

A team consisting of a paediatrician, an otologist, an educational psychologist and an audiology technician were given facilities for carrying out detailed clinical examinations and hearing tests at the Province of Natal Welfare Centre of the Institute of Child Health in Bloomsbury, London.

The children selected for this examination were those whose mothers had rubella during the first 18 weeks of pregnancy and who lived in the London area in the counties of London and Middlesex. A total of 57 such children were examined, together with an equal number of matched controls. The ages of the rubella group ranged from 3 years 3 months to 5 years 1 month (mean age 3 years 11 months); for the control group the range was 3 years 6 months to 5 years 6 months (mean age 4 years 2 months). In each group there were 30 boys and 27 girls. The names were supplied by the General Register Office from the national list and arrangements to attend for examination were made by the Divisional and Area Medical Officers of the London and Middlesex County Health Departments.

A detailed history was taken, and a full general examination carried out by a paediatrician. The hearing tests were carried out in the usual manner, as

applicable to very small children, that is, the child was "conditioned" to carry out a certain action in response to sound, and when full conditioning was achieved, the hearing was tested by a variety of sounds of low and high frequencies in free field. The same method of "conditioning" in a play situation was used for audiometry, and the aim was to carry out a full audiometric test in all children. The audiometrician who carried out the tests had no knowledge to which group the children belonged, in order to eliminate any possibility of bias. Reliable audiograms were obtained in all except seven of the 114 children examined, and in these seven the results of voice tests were considered adequate for deafness to be confirmed or excluded. Voice tests were carried out in all children. A full otological examination was carried out. A full description of the methods used and an extensive review of the cases of deafness which were found has been published elsewhere²⁹.

The results of the investigation are summarized in the tables which follow.

Table 33. Findings in 57 children following maternal rubella in the first 18 weeks of pregnancy

							<i>No. of cases</i>	
Unilateral cataract, microphthalmos, nystagmus	1	
Unilateral cataract, congenital heart disease (? pulmonary stenosis), congenital deafness	1	
Mental defect, congenital deafness	1	
Congenital deafness alone	12	
Total number of children with major congenital defects	15	
Slight conductive deafness	5	
Large hairy mole over sacrum	1	
Epilepsy (petit mal)	1	
Small flat pigmented mole on hand	1	
No abnormality	34	
Total	57	

Table 34. Findings in 57 control children

							<i>No. of cases</i>	
Mild congenital deformity of skull (dolichocephaly)	1	
Slight conductive deafness	5	
No abnormality	51	
Total	57	

Table 33 shows the defects detected in the 57 children of the rubella group. In this group there were 15 children with major congenital defects (including all degrees of congenital deafness) which probably resulted from maternal rubella. None of the major defects other than deafness had escaped recognition at the examinations of the national enquiry. In addition there were 3 children with minor congenital defects and 5 with slight hearing defects of an acquired type. In the control group only one child had a minor congenital defect, but here again there were 5 children with acquired hearing defects of a trivial nature. (Table 34).

*Table 35. Major congenital defects:
Week of pregnancy in which maternal rubella occurred*

<i>Defect</i>	<i>Week of pregnancy</i>
Unilateral cataract, microphthalmos, nystagmus (1 case)	4th
Unilateral cataract, congenital heart disease (? pulmonary stenosis), congenital deafness (1 case)	9th
Mental defect, congenital deafness (1 case)	12th
Congenital deafness alone (12 cases)	6th-14th

Table 35 shows the week of pregnancy (calculated from the first day of the last menstrual period) in which maternal rubella occurred for the 15 children with major congenital defects.

Table 36. Distribution of 57 cases in rubella group according to week of pregnancy in which maternal rubella occurred

<i>Week of pregnancy</i>	<i>Children with major congenital defects</i>	<i>Children with no major congenital defects</i>
0-3rd inc. ..	0	4
4th	1	3
5th	0	3
6th	1	0
7th	0	2
8th	0	4
9th	1	2
10th	3	2
11th	1	2
12th	6	3
13th	1	4
14th	1	0
15th	0	1
16th	0	1
17th	0	6
18th	0	5
Total	15	42

Table 36 gives the distribution of maternal rubella during the first 18 weeks of pregnancy with the incidence of normal and affected children. In this selected group major congenital defects did not arise when maternal rubella occurred before the 4th or after the 14th week of pregnancy. During the first 16 weeks of pregnancy there were 46 children at risk, of whom 15 (32.6 per cent) developed major congenital defects and 31 (67.4 per cent) did not.

Table 37. *Types of deafness*

							Rubella group	Controls
Number of children examined							57	57
Slight acquired conductive deafness							5 (8.8%)	5 (8.8%)
Severe congenital perceptive deafness	Unilateral						14 (24.5%)	0
	Bilateral (one ear only slightly affected)							
	Bilateral (both ears severely affected)							

The details of cases of deafness in both rubella and control groups are shown in Table 37. In each group there were 5 cases (8.8 per cent) of slight acquired conductive deafness. This is a higher incidence of conductive deafness than is usually found on routine testing, for example of school-children, and is probably explained by the insistence on obtaining reliable audiograms in the present investigation, and the strict criteria used in the assessment of deafness. A hearing loss of 20 decibels or more in at least two adjacent frequencies or a loss of 30 decibels or more in a single frequency was considered to be significant deafness. The hearing loss in the cases of conductive deafness was only slight or moderate and caused no disability. Nevertheless it is important to detect and to treat or follow up such deafness which may be the early stage of a progressive lesion.

In the 7 children for whom reliable audiograms could not be obtained the assessment of hearing was based on voice tests alone. Two of these children had severe bilateral deafness, but it was not possible to exclude minor degrees of hearing loss in the remainder, who were considered to have normal hearing.

The most important feature of the investigations was the finding of 14 cases (24.5 per cent) of severe congenital perceptive deafness in the 57 children of the rubella group. This deafness was unilateral in 5 cases; in 3 cases there was bilateral deafness but the hearing loss in one ear was only slight or moderate. Severe deafness in only one ear does not usually affect hearing for speech but in unfavourable circumstances may be almost as serious a handicap to a child as bilateral deafness.

The remaining 6 cases of congenital deafness were bilateral with severe impairment of hearing in both ears. This is the type of deafness which has been more commonly found in children with the "rubella syndrome" and is a most

Table 38. *Incidence of previously undiagnosed deafness*

	Rubella group		Controls	
	Previous diagnosis	Undiagnosed	Previous diagnosis	Undiagnosed
Acquired deafness ..	0	5	0	5
Congenital deafness ..	5	9	0	0
Totals .. .	5	14	0	5

serious handicap. Unless special measures are taken at a very early age children with such severe deafness will probably not acquire natural speech, and even if they are of normal intelligence will suffer serious educational deprivation. They are often referred to as deaf-mutes.

The particular value of this special investigation is indicated by the number of affected children in whom the deafness was not detected or even suspected at the routine one-year and two-year examinations of the national enquiry. The relevant figures are given in Table 38. In only 5 out of a total of 24 children with hearing loss had the diagnosis been made before the present examination. These were, of course, the children with the most severe bilateral congenital deafness whose symptoms had aroused suspicion at an early age. All the undiagnosed cases, including one child with moderately severe bilateral deafness, had few or no symptoms. On the routine clinical examinations deafness was not, therefore, suspected and hearing tests were not carried out.

It is not surprising that the 10 cases with slight and probably variable conductive deafness had escaped detection. Even severe deafness which is mostly or entirely unilateral causes little disability before school age and is difficult to detect in young children without the aid of audiometry. In one child quite severe unilateral deafness had escaped notice although two other defects (cataract and congenital heart disease) were known to be present. The only child with undetected severe bilateral deafness had, in fact, some residual hearing and had learned to talk. Unless the possibility of deafness is constantly borne in mind and hearing tests are carried out on the slightest indications the diagnosis will be missed, at any rate at the age at which these children were examined.

The high incidence of undetected congenital deafness disclosed by this investigation and the fact that deafness is so frequently the only defect (12 out of 14 cases) indicate the necessity for detailed hearing tests as early as possible in all children whose mothers have had rubella in the first 4 months of pregnancy.

The results of a statistical analysis of the birth weights and of the weights, heights, and head circumferences measured at the time of examination are presented in tables 39, 40 and 41. Those children from the rubella group for whom data were incomplete were excluded, leaving 40 cases with no congenital defects and 11 with congenital deafness only.

Table 39. Comparison of birth weights and physical measurements in rubella cases without congenital defects and controls

	No.	Mean birth weight (lb.)	Mean exam. weight (lb.)	Mean exam. height (ins.)	Mean exam. head circ. (ins.)	Mean exam. age (years)
Rubella cases	40	7.05	34.93	39.54	19.83	3.90
Controls	40	7.53	36.34	39.93	19.89	4.08
Difference of means: rubella-controls ..		-0.48	-1.41*	-0.39**	-0.06	-0.18
t†		1.5	0.85	0.64	0.33	1.74

* Add 0.7 lb. for age adjustment

** Add 0.4 ins. for age adjustment

† Ratio of difference to its standard error (significant at 5 per cent level when $t > 2$)

Table 39 shows the comparison between the 40 children without congenital defects and 40 controls, matched exactly for sex (21 males, 19 females) and as closely as possible for age (mean age of controls 0.18 years greater than mean age of rubella group). The mean birth weight was approximately $\frac{1}{2}$ lb. greater in the control group but this difference was not statistically significant. The differences for physical measurements were very small and are even smaller when the figures are adjusted for the difference in mean age between the two groups.

Table 40. Comparison of birth weights and physical measurements in rubella cases with deafness and controls

	No.	Mean birth weight (lb.)	Mean exam. weight (lb.)	Mean exam. height (ins.)	Mean exam. head circ. (ins.)	Mean exam. age (years)
Rubella deaf	11	6.81	33.34	39.34	19.55	3.82
Controls	11	7.64	37.20	39.57	19.80	3.85
Difference of means: deaf-controls		-0.83	-3.86	-0.23	-0.25	-0.03
.. .. .		1.49	2.66	0.36	1.10	—

Table 41. Comparison of birth weights and physical measurements in rubella cases with deafness and rubella cases without congenital defects

	No.	Mean Birth weight (lb.)	Mean exam. weight (lb.)	Mean exam. height (ins.)	Mean exam. head circ. (ins.)	Mean exam. age (years)
Rubella deaf	11	6.81	33.34	39.34	19.55	3.82
Rubella (no defects) ..	11	7.39	36.02	39.70	20.00	3.83
Difference of means: deaf-no defects ..		-0.58	-2.68	-0.36	-0.45	-0.01
.. .. .		1.03	1.64	0.48	1.49	—

In tables 40 and 41 eleven deaf children from the rubella group are compared with 11 rubella cases without defects and 11 controls, all three groups being closely matched for age and sex (7 males, 4 females). The deaf group weighed significantly less than the controls at the time of examination. None of the other differences were significant but most of the figures were smaller for the deaf group than for both the other groups.

SECTION II

The re-examination described in Section I above, of a sample of children whose mothers had rubella in the early months of pregnancy had shown at three to five years of age a much higher incidence of deafness than had been found or even suspected on medical examination at two years of age. All the previously undiagnosed cases had few or no symptoms so that on routine clinical examinations deafness would not be suspected. No other major congenital defects were

discovered—a fact which testified to the high standard of the original examinations.

Because of this new-found high incidence of impairment of hearing it was thought that all the children whose mothers were known to have had rubella in the early months of pregnancy should be re-examined so that those with defective hearing might begin special training as early as possible. In July, 1957, Medical Officers of Health were advised of these findings and were given copies of the original completed record cards of the children in their areas who were known to be at risk. Medical Officers of Health were asked to be good enough to return the record cards with information of further examinations.

There were in the rest of England and Wales 212 children and in Scotland 12 children whose mothers were recorded as having had rubella during the first 18 weeks of pregnancy. These included children of mothers selected during 1953 in the few Local Health Authority areas wherein selection of rubella cases continued for a year after the main enquiry ended. Medical Officers of Health in England returned the record cards of 191 children and from Scotland 11 cards were returned. The families of three English children had left the country, the parents of nine children refused, or did not attend for examination, seven children could not be traced and two children were unco-operative and would not submit to examination: 170 children were re-examined. In Scotland ten children were re-examined and one could not be traced.

Table 42. Re-examination of Rubella Children between three and seven years of age.
Re-examination reports in italics; reports of previous examinations in normal print

(a) Children with hearing defects:

Case No.	Week in pregnancy when rubella occurred					Birth weight lb. oz.	Defects			
	0-4th	5th-8th	9th-12th	13th-16th	17th-18th		Mental	Heart	Eye	Ear
6034	1st					5 8	General backwash Mentally backward	Congenital heart	Contract	Marked hearing loss.
5947	3rd					7 8				Deafness both ears (Audiologist states not due to rubella).
5397	4th					4 14				Marked low tone deafness, both ears.
6193	4th					8 5				Deafness speech defect, deafness, right ear.
6173	5th					3 13		Heart operation Congenital heart		Partially deaf. Speech very backward.
6440	5th					2 12				Slight deafness, right ear. Started to have infection, middle ear, at birth.
6208	6th					7 4				Not completely, but very deaf. Not speaking at all may be congenitally deaf.
6270*	6th					4 4	(Normal intelligence) Very backward, no words spoken			Small pale child, deaf, wears hearing aid.
6041	7th					7 1				Severe deafness, advised special school. Impaired hearing.
6391	8th					4 13				Almost complete deafness—in special school. Deafness.
6114	8th					4 15				Some hearing loss, "extremely unlikely to be due to rubella".
6225	8th					6 31				High frequency deafness—wears hearing aid. Severely deaf; in residential school for deaf.
6480	8th					8 8				Weighted only 22 lb. at 2 years.

Some affection of lower limbs. Calipers abandoned; not a spastic condition. ? spasticity, lower limbs.

Weighted only 22 lb. at 2 years.

Table 42. (contd.)

Case No.	Week in pregnancy when rubella occurred				Birth weight lb. oz.	Defects			
	0-4th	5th-8th	9th-12th	13th-16th		Mental	Heart	Eye	Other
6261		12 ^x			7 2	(High intelligence)			Defective hearing, right ear—? due to inflammation or rubella.
6436		12 ^x			6 4	Probably mentally backward for Special School. Intelligence may be sub-normal.			Partial deafness—bilateral, more severe, slow in all ways.
5977			15 ^x		7 3				Hearing just sub-normal.
6366			15 ^x		6 4				Slight bilateral conductive type of deafness— "No connection with rubella".
6467			15 ^x		7 0				Partial deafness—Special relation and attended ordinary school.
6463			15 ^x		6 8	Mental Defective, in Occupation Centre			Very slightly deaf.
6209			15 ^x		9 0	Backward child			Mild conductive deafness, both ears, detected only by audiometry. Heeds normal conversation.
(b) Other reports.									
5932		9 ^x			5 14			Conductive Operative Left ear	Very severe child. Retarded development.
6286*			13 ^x		6 13		Very high systemic anomaly, of no significance Congenital heart		(No hearing loss). ? hearing.
6013*			13 ^x		8 0				(Nil)
6094				17	6 8				(Nil)
6039		10 ^x			8 0		Congenital heart		(Nil)
6123		5 ^x			6 5			Bilateral cataract	Cleft palate. Pyloric stenosis.

x—infection confirmed by doctor. m—infection mild. M—infection moderate.

*—diagnosis made at 2 years has been altered on examination later.

S—infection severe.

Reports of the examination of 180 children aged between three and seven years show that 156 had no serious defects. Twenty-four had major defects as shown in Table 42. Twenty children had deafness of varying degree: in only seven of these had deafness been diagnosed or suspected on examination at two years of age. The defects in the other four children had been recorded at earlier examinations. Three previous diagnoses have now been altered. One child who was very backward and was included in the original analysis as mentally retarded was now found to be deaf and of normal intelligence. The second child, originally stated to have congenital heart disease was now found to have only a systolic murmur of no significance. The third child in whom deafness was suspected has normal hearing.

Table 43. Cases of deafness found amongst the children (aged 3-7 years) of mothers who had Rubella during first 18 weeks of pregnancy

Whole Country

Stage when rubella occurred						Number of cases	No deafness	Slight deafness	Severe deafness	Total deaf
1st week	10	9	0	1a	1
2nd week	2	2	0	0	0
3rd week	7	6	0	1c	1
4th week	7	5	1b	1	2
Total to 4th week						26	22	1 3.6%	3 11.5%	15.4%
5th week	11	9e	2d	0	2
6th week	8	6	0	2	2
7th week	5	4	0	1	1
8th week	14	10	2c	2	4
Total 5th-8th week						38	29	4 10.5%	5 13.2%	9 23.7%
9th week	5	3e	0	0	0
10th week	7	7f	0	0	0
11th week	15	15	0	0	0
12th week	15	13	2g	0	2
Total 9th-12th weeks						42	40	2 4.8%	0	2 4.8%
13th week	7	7	0	0	0
14th week	13	13	0	0	0
15th week	20	15	5h	0	5
16th week	10	10	0	0	0
Total 13th-16th weeks						50	45	5 10.0%	0	5 10.0%
17th week	8	8j	0	0	0
18th week	16	16	0	0	0
Total 17th-18th weeks						24	24	0	0	0
Total 0-18th weeks						156	135	12 7.7%	8 5.1%	20 12.8%

a one case of deafness "not due to rubella."

d congenital heart, cataract and general backwardness.

e enlarged spleen and erythroblastosis.

f one case with congenital heart and cataract.

g one has congenital heart.

h one case with cataract.

i one case pyloric stenosis.

j one case probably mentally backward.

k one case mental defective.

l one case cleft palate.

Table 43 shows the number and percentage of deaf children related to the time in pregnancy when rubella occurred.

Of the 20 deaf children eight were severely or markedly deaf and twelve were partially or slightly deaf. One case of severe deafness and one of slight deafness were, the audiologist stated, not due to the rubella infection and a third case had "some hearing loss extremely unlikely to be due to rubella". Five deaf children had other congenital defects. One severely deaf child who was generally backward had congenital heart disease and cataracts and at birth had suffered from thrombocytopenic purpura. Another had a hypotonic affection of the lower limbs. One partially deaf child had congenital heart disease, a second was probably mentally backward and a third had purpura and erythroblastosis shortly after birth. Two of the deaf children were stated to be undersized.

All the 20 cases of deafness occurred amongst the 156 children whose mothers had rubella within the first 16 weeks of pregnancy—an incidence of 12·8 per cent, 5·1 per cent being severely deaf and 7·7 per cent being only partially deaf. The highest incidence of deafness, and all the severe cases, followed rubella in the first eight weeks of pregnancy: of 64 children 13, 20·3 per cent were deaf—12·5 per cent were severely deaf and 7·8 partially or slightly deaf. When rubella had been between the 9th and 16th weeks 7 of 92 children, i.e. 7·6 per cent were partially deaf. There were no deaf children amongst the 24 whose mothers had rubella during the 17th and 18th weeks of pregnancy.

Unlike the re-examinations in London and Middlesex described in Section I there are no comparable re-examinations of control children. In the London and Middlesex examinations an equal number of children with acquired hearing defects was discovered in the rubella and in the control groups. It is reasonable to assume that, at least, a few of the hearing defects found in the country as a whole are of an acquired type and are not due to rubella. In fact in three cases the audiologist reported that deafness was not due to rubella infection and in two other cases rubella was a doubtful agent.

In the analysis of the results of the main inquiry the incidence of deafness amongst children whose mothers had rubella in the first 12 weeks of pregnancy was 2·7 per cent with a possible increase of 3·3 per cent, if cases of suspected deafness were included.

Altogether 202 children in the rubella group, where the infection had been within the first 16 weeks of pregnancy, have been re-examined after the age of 2 years and a summary of the deaf cases found at these examinations, described in Sections I and II above, is given in Table 44.

Table 44. Cases of deafness found at latest re-examinations

Week in pregnancy of rubella	Children in Middlesex and L.C.C.			Children throughout Country			All children		
	Total examined	No.	%	Total examined	No.	%	Total examined	No.	%
0-4	8	0		26	4	15·4	34	4	11·8
5-8	10	1	10·0	28	9	32·1	48	10	20·8
9-12	20	11	55·0	42	2	4·8	62	13	21·0
0-12	38	12	31·6	106	15	14·2	144	27	18·8
13-16	8	2	25·0	50	5	10·0	58	7	12·1
0-16	46	14	30·4	156	20	12·8	202	34	16·8
17-18	11	0		24	0		35	0	

VI. DISCUSSION

The present investigation aimed at obtaining information about a number of normal pregnancies and pregnancies complicated by certain virus diseases, large enough to yield statistically significant results. It was therefore on a national scale, covering England, Wales and Scotland, and the selection of cases continued during two-and-a-half years. Enquiry was entirely prospective. All complicated pregnancies were registered at the General Register Office before termination whether by miscarriage, still birth or live birth; registrations received after the date of termination were discarded. Thus every case included in the final analysis had been selected and registered before the birth of the child. Diagnosis of virus infection was confirmed in most cases by a doctor. Live-born children were examined at birth, one year, and two years of age. A control series of uncomplicated pregnancies selected as described earlier in this report was observed in exactly the same way. In some parts of the country additional pregnancies complicated with rubella continued to be selected for a year after the main enquiry had ended but these are not included in this analysis as control pregnancies were not also selected (see appendix). The final analysis included 578 rubella, 103 measles, 501 mumps, 298 chickenpox, 33 poliomyelitis and 5,717 control cases. One hundred and sixty six cases of influenza during pregnancy selected in two areas during a severe epidemic in 1951 are also included. Subsequent to the main enquiry arrangements were made for the re-examination at ages three to seven years of all the children whose mothers had rubella during the first 18 weeks of pregnancy.

Rubella

Of the 578 rubella pregnancies 202 had infection in the first 12 weeks, 276 between the 13th and 28th weeks and 96 between the 29th and 40th weeks. It is difficult to account for the preponderance of infections during early and mid pregnancy as recorded in our enquiry and remarked upon by other observers. It may be that expectant mothers go about more freely than in late pregnancy and so may be more likely to come in contact with infection. Or perhaps, as a result of the general knowledge gained from press and radio that infection during late pregnancy is of little or no importance, such cases tend to go unrecorded. In the present investigation the later in pregnancy infection occurred the greater would be the chance of a lost case due to registration not being received until after the birth of the child.

The relative wastage by abortion and still birth and infant death and the condition of the live born children of rubella and control pregnancies are shown in Tables G and L and Figures 1 and 2 (pages 22-34).

The rubella cases showed the now familiar pattern of an increase in the expected number of abortions, still births and malformed children when infection was in early pregnancy. The danger period was the first 16 weeks, the first 12 bearing most of the casualties and the 13th to 16th comparatively few. Rubella during the later weeks of pregnancy did not appear to alter the normal course of events.

Of 202 cases of infection within the first 12 weeks 10 ended in abortion and 9 in still birth. The percentages of abortions compared with the controls were 5.0 and 2.4 and of still births 4.5 and 2.4. The pre-natal deaths, i.e. abortions and still births, were almost twice as many as the control series would lead one to expect. The greatest number of still births followed rubella in the first 8 weeks, 7.5 per cent compared with an expected 2.7 per cent. There was no increase in abortions when rubella occurred later than the 12th week. There was an isolated and presumably fortuitous increase in still births when rubella was between the 29th and 32nd weeks. The percentage of still births, 4.5 in this series of first trimester infections, is lower than that found in most other prospective investigations. Greenberg *et al* summarised 125 cases from their own and other prospective investigations of which 7.2 per cent ended in still birth.

In the present enquiry the increase in abortions and still births in first trimester rubella cases resulted in fewer live births, 90.5 per cent compared with 95.2 per cent in the control series. The infants of these rubella pregnancies were generally smaller than those of control pregnancies; 17.7 per cent of those born after the 36th week of pregnancy weighed 5½ lbs. or less at birth compared with 4.3 per cent of control infants. There was no such difference when rubella occurred later than the 12th week in pregnancy.

There was a high infant mortality of rubella infants. Of 547 live births 24 infants died within a year but there were no deaths during the second year of life. The infant mortality rates per 1,000 live births were 43.9 in the rubella group, 25.8 in the control group and the national rates for the years concerned were between 29.7 and 26.8. Fourteen, more than half, of the rubella deaths were of children whose mothers had rubella within the first 12 weeks of pregnancy which represented an infant mortality rate of 76.5, almost three times as high as would normally be expected. When infection occurred after the 12th week it was only between the 21st and 24th weeks that the deaths were in excess, four as compared with an expectation of 1.9. It is doubtful if this is of any significance.

The rubella infant deaths differed from those in the control series in two respects; there were more malformed children and a higher incidence of prematurity. Eleven of the rubella infants who died had major malformations, 46 per cent compared with 34 per cent in the control group. In seven of the 11 malformed children rubella had been within the first 12 weeks of pregnancy. Five of these children had heart defects, in two associated with cataract and in a third with multiple deformities. The incidence of cardiac defects in the rubella children who died was more than twice that in the control series so it is likely that at least some of these defects may be attributable to rubella infection.

Of control infants born after the 36th week of pregnancy and who died under two years of age 19 per cent with no major defects and 21 per cent with major defects weighed five and a half pounds or less at birth. The corresponding percentages of all rubella infant deaths were 27 and 67, and of those in which rubella had been within the first 12 weeks of pregnancy 40 and 85.

Although other observers have reported infant deaths following rubella in pregnancy their cases were so few that no real estimation of this risk could be made. From the present series it appears that if rubella occurs within the first 12 weeks of pregnancy a live-born infant is almost three times more likely to die in the first year of life than if there were no history of maternal rubella.

As a result of the high number of pre-natal and infant deaths our figures indicate that of 100 women who had rubella in the first 12 weeks of pregnancy, 84 might have children alive at 2 years of age, instead of 93 had there been no maternal infection.

The last medical examination of all the children included in the main investigation was carried out when they were two years of age. Gross deformities including those of heart and eye would be obvious then but defects such as impairment of intelligence and hearing might not be. That this was so was shown by later examination of some of the children when aged between three and seven years when no new major defects were found except those of hearing and in a few instances, of intelligence. It is therefore reasonable to suppose that apart from these two types of defect the present investigation gives realistic evidence of the rubella risk. It does not give any information in detail of the lesions described as cardiac and eye malformations. It was not intended to do so. The main object was to determine if possible to what extent rubella in pregnancy interfered with the normal course of events, and to do this a large number of cases was required. The very extent of the enquiry made for limitations. It was not possible to get detailed clinical reports about so many children in so many different places. Perhaps further studies can be made.

Thirty-seven of the live-born rubella infants had major malformations, 6.8 per cent compared with 2.3 per cent of control infants, but the high incidence of malformations in the rubella group was preponderantly when the infection in the mothers had been within the first 12 weeks of pregnancy, 15.8 per cent, and to a much lesser extent, 4.2 per cent, when between the 12th and 16th weeks. There was no increase in the number of malformed children when infection was later in pregnancy. Thus, of 183 infants whose mothers had rubella during the first 12 weeks of pregnancy 154, or 84.2 per cent, had no major abnormalities. This compared with 97.6 per cent in the control group.

Malformations of the heart, eye, ear and brain which singly or in combination have been associated with maternal rubella were found in 25 of the 37 malformed children. In all but two of these 25 cases rubella had been within the first 12 weeks of pregnancy: one of the exceptions, a child whose mother had rubella at the 13th week of pregnancy and reported at two years of age to have congenital heart disease, was at a later examination found to have only "a slight systolic murmur of no significance"; the other was a mentally defective and slightly deaf child whose mother had rubella at the 15th week of pregnancy. Malformations which appeared following rubella after the 16th week in pregnancy showed no special characteristics.

Malformations of the heart were the most common, 14 children being so afflicted, and in all but one case (that mentioned in the preceding paragraph) the maternal infection had been within the first 12 weeks of pregnancy. The incidence of cardiac defects in children of mothers with first trimester infections was 7.1 per cent. Figure 3 shows that the highest incidence was found when infection had been in the first eight weeks of pregnancy. Cardiac malformations were present in 26 of the control children, an incidence of 0.5 per cent. Of the 14 rubella children seven had only a cardiac defect and seven had associated defects, cataract in six cases.

- 1 Heart. Cataract. Mentally backward (rubella 1st week of pregnancy)
- 2 " " Porencephaly (4th week)
- 3 " " Deaf (9th week)
- 4 " " (5th week)
- 5 " " (5th week)
- 6 " " (9th week)
- 7 " and multiple deformities (3rd week).

Only four of the 26 control cardiac cases had associated defects, (1) hydrocephalus, (2) congenital nystagmus, (3) hypertelorism, (4) Hirschsprung's disease.

Gregg had observed that rubella infants with cardiac disease were usually small. In our series eight of the 14 affected children weighed $5\frac{1}{2}$ lbs. or less at birth, compared with three of 26 in the control group. Despite this additional handicap, mortality amongst the rubella heart cases was less than amongst the controls. Just over one-third of the rubella cases and over one-half of the control cases died before two years of age.

Cataract, the second commonest malformation occurred alone in four cases and in association with heart malformations in six cases all when rubella had been within the first nine weeks of pregnancy. There were two children with cataract and two with defective vision in the control series, an incidence of 0.07 per cent. In rubella children with maternal infection within the first 12 weeks the incidence of eye defects was 5.5 per cent. Figure 3 shows the highest incidence when rubella had been in the first four weeks of pregnancy.

Four children showed mental defects of varying degree, in one case associated with congenital heart and cataract. In all cases rubella was within the first 16 weeks of pregnancy (one in each four-week period), an incidence of 1.5 per cent compared with 0.4 per cent in the control children.

Five rubella children had some degree of deafness, one of whom had also congenital heart and cataract—in all cases rubella was within the first 12 weeks of pregnancy, an incidence of 2.7 per cent compared with 0.07 per cent in the control group. Deafness was suspected in six other rubella children and three were backward so the incidence might be higher by 1.6 per cent in all rubella children or 3.3 per cent in those whose mothers had rubella in first 12 weeks of pregnancy. Figure 3 shows that the greatest proportion of deaf and suspected deaf children occurred amongst those whose mothers had rubella between the 5th and 12th weeks of pregnancy.

Re-examination of rubella children between the ages of three and seven has brought to light many more cases of deafness. In the controlled study in London and Middlesex described in Chapter V, Section I, 30 per cent of children whose

The figures shown on the columns are percentages

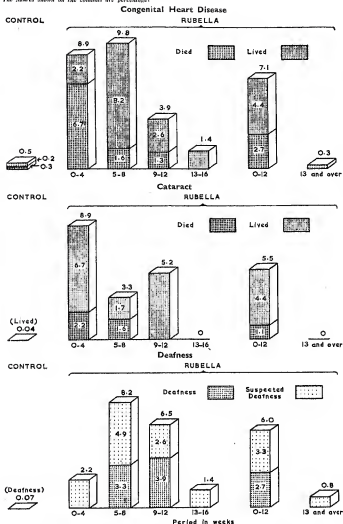


Fig. 3. Incidence of Congenital Heart Disease, Cataract and Deafness, observed before the age of 2 years, in live born infants in the rubella series, (according to the stage of pregnancy when rubella occurred), and in the control series; infants dying under 2 years of age are distinguished.

mothers had rubella in the first 16 weeks of pregnancy had impaired hearing—the highest incidence appeared when rubella had been between the 10th and 12th weeks.

The re-examination of rubella children throughout the country described in Chapter V, Section II, showed an impairment of hearing in 12·8 per cent of the children whose mothers had rubella within the first 16 weeks of pregnancy—the highest incidence, 20·3 per cent occurred when rubella was within the first eight weeks of pregnancy. From these two studies it is obvious that the risk of deafness following maternal rubella in the first 16 weeks of pregnancy is considerably higher than our original finding of from 2·7 to a possible 6·0 per cent. It would seem to be between 13 and 30 per cent. But it should be appreciated that not all the affected children are severely handicapped—about two-thirds are attending ordinary schools. All the severe cases of deafness followed rubella within the first 12 weeks of pregnancy. Of the 34 deaf children found in the two recent studies 27 had no other defect.

Other malformations seen in the rubella children occurred so infrequently that it is not possible to assess their significance. An exception perhaps may be made of the three cases of atresia of the oesophagus or intestine which occurred in children whose mothers had rubella in the 5th, 9th and 15th weeks of pregnancy. Only one case was reported in the control series so the incidence when rubella had been within the first 16 weeks of pregnancy was 1·2 per cent compared with 0·02 per cent in the control series.

Individual published studies of prospective investigations deal with such small numbers of rubella pregnancies that some writers have pooled the results of several such studies in order to determine the over-all risk of rubella in pregnancy. Ingalls in 1953 summarized the American studies which had produced altogether 72 cases of rubella in pregnancy and found in first trimester cases a risk of 9·5 per cent still births and 7 per cent malformed children. In 1957 he included further cases making in all 100 and found the first trimester risk 6·3 per cent still births, 15·9 per cent malformations, the second trimester 7·1 per cent still births and 14·3 per cent malformations: there were no still births nor malformations in third trimester cases.

Greenberg *et al.* New York, 1957, reported malformations in 3 of 31 live-born infants of women who had rubella in the first trimester, i.e. 9·7 per cent. He also summarized previous studies finding first trimester risk 7·2 per cent still births, 12 per cent malformations, second trimester 4·6 per cent still births, 3·8 per cent malformations, and third trimester 1·7 per cent still births, malformations nil.

Bradford Hill, 1957, found 44 cases of rubella during pregnancy. Of 18 first trimester cases there were four and possibly 5 children with malformations, i.e. 22 to 28 per cent. Of 15 second trimester cases there was one child with major malformation and one still birth. Of five third trimester cases there were no malformations. He also summarizes his own and three other studies showing the risk of rubella in the first month to be 50 per cent malformations in second month 25 per cent malformations, in third month 17 per cent, in fourth month 11 per cent and fifth and sixth months 6 per cent.

In the present controlled investigation rubella apparently affected the foetus only when it occurred within the first 16 weeks of the pregnancy. The risks involved when infection was within each four weekly period are shown in

Figure 4. Of 100 women who had rubella in the first four weeks 80 had children alive at two years of age, 8 of whom had major defects. When rubella was between the fifth and eighth weeks there were 81 children of whom 13 were malformed. When rubella was between the ninth and twelfth weeks there were 88 children of whom 11 were malformed and when between the 13th and 16th weeks there were 93 children of whom three were malformed. Women with uncomplicated pregnancies had 94 children of whom one or two were malformed.

Re-examination of the rubella children between the ages of three and seven has brought to light no new defects except those of deafness. These new cases add considerably to the rubella risk of malformation. From the information received from Medical Officers of Health throughout the country and from Dr. Jackson and Dr. Fisch's study, (altogether 237 rubella children were re-examined), it appears that when the infection had been within the first 12 weeks of pregnancy the incidence of deafness, either slight or severe, was 18.8 per cent; when the infection occurred between the 13th and 16th weeks the incidence was 12.1 per cent and in no instance was the defect severe.

The risk of defective children following rubella in the first three months of pregnancy is relatively high but it should be remembered that by no means all of the defective children were severely handicapped. Operative treatment had been successfully carried out on some of the children with heart and eye defects; about two-thirds of the deaf children were able to attend ordinary schools. Only a few children had multiple defects of heart, eye, hearing or intelligence. Mental defects although more frequent in rubella children than in control children were not common. We have no evidence as to whether rubella children differ in temperament and behaviour from other children as some observers believe to be the case. But we have heard of one child who is a nervous wreck because of his mother's anxiety and belief that he is different from other children because of her infection during pregnancy and the paediatrician is finding it very difficult to convince her that her child is quite normal. Occasionally an examiner has remarked on the high intelligence of a rubella child. It has been stated that rubella in pregnancy is associated with spastic children but there was no spastic child in our rubella group.

Rubella infection during pregnancy is so rare, in this country at any rate, that its ill effects upon the foetus are not a significant cause of congenital malformations in general. From the number of affected pregnancies and control pregnancies which were reported in England, Wales and Scotland during two and a half years it is estimated that during a non-epidemic year about 200, and during an epidemic year not more than 2,000, pregnant women might be expected to suffer from rubella and the foetus would be at risk only if the infection occurred during the first trimester. Nevertheless to the pregnant woman an attack of rubella during the early months is a matter of grave import, causing at least anxiety, and at most a defective child. It is therefore important to protect pregnant women against attacks of rubella.

Other virus infections

None of the other virus infections during pregnancy produced such obvious deleterious effects on the foetus as did rubella, and further investigation on a much larger scale would be necessary before such mishaps as did occur could be attributed directly to the respective virus infections.

There is no evidence whatever of any harmful effect to the child following chickenpox or mumps during pregnancy.

In the present series of cases of measles in pregnancy there was both a higher infant death rate and a higher number of malformed children than would be expected. The infant death rate was particularly high after measles in the first twelve weeks of pregnancy, when six out of the 35 live born infants died before they were two years old. Only one death would be expected in a group of this size. The higher rate of malformations, 7 per cent compared with 2 per cent in the controls, was not confined to any particular period in pregnancy. It is difficult to accept these findings as fortuitous, but equally difficult, in view of the small number of cases involved, to know to what extent they indicate a real danger to the foetus. It is possible that there was confusion about the diagnosis and that some of the cases were in fact rubella and not measles. One of the children had a "rubella-type" defect,—a combination of a heart and eye defects—but there is little else in the outcome of the measles cases to suggest a large-scale confusion with rubella. In conclusion it can only be said that it is possible that measles during pregnancy has harmful effects on the child, but the evidence is not strong.

In the group of poliomyelitis cases the outcome of the six cases in which poliomyelitis occurred between the 9th and 12th weeks of pregnancy was remarkably poor—there was one abortion, two still births, and one live-born child with a major malformation who died at the age of one week, only two children surviving to two years. In spite of the very small number of cases involved it appears that poliomyelitis during pregnancy may have some damaging effect on the foetus—perhaps not surprisingly, in view of the seriousness of the disease. The one malformation in the series—hydrocephalus with spina bifida is one which occurred frequently in the control series and probably indicates nothing specific.

The outcome of the influenza series presented only one note-worthy sequence. When influenza occurred between the 13th and 28th weeks, five out of the 97 live born infants died before they were two years old, from a variety of unremarkable causes. Only two or three deaths would have been expected. It is difficult to accept this as evidence of a risk to the child following influenza in pregnancy but the possibility cannot be dismissed. No more definite conclusion can be reached at present.

The 1951 influenza epidemic, on which these observations were based, was due to virus A prime. More recently several investigators have studied the effects of the outbreak of Asian influenza of 1957, with conflicting results. Coffey and Jessop²⁰ reported an increased incidence of congenital malformations in a maternal influenza group of children compared with controls, and Pleydell²¹ found a higher incidence of malformations and abortions. On the other hand neither Walker and McKee²² nor Wilson and co-workers²³ found any evidence of foetal damage due to the Asian influenza virus.

SUMMARY

Following the Australian observations early in the 1940's suggesting a high incidence of congenital malformations in children whose mothers had contracted rubella early in their pregnancy, and indications from later small series that the

risk might not be so high as originally feared, a full-scale investigation was started in mid-1950 by the Ministry of Health and the General Register Office with the co-operation of the Department of Health for Scotland and Medical Officers of Health in England, Wales and Scotland, with the object of obtaining information about the outcome of a large number of pregnancies complicated by rubella and other virus infections, and comparing them with the outcome of a large control series. Women who contracted rubella, measles, chickenpox, mumps or poliomyelitis during pregnancy were registered until the end of 1952. In addition, some cases of influenza in pregnancy were registered during an epidemic in Manchester and Liverpool in 1951 and some further cases of rubella were registered in certain areas in 1953. The enquiry was a prospective one and fulfilled the desiderata set out by Logan in 1951. The random control group, about ten times as large as the series of rubella cases, consisted of women who did not suffer any of these infections during their pregnancy and whose birthday fell on the 31st of a month. After a case was selected, a registration card giving brief details was sent to the General Register Office. No case was included in the survey unless this card was received there before the end of the pregnancy and no change of opinion on the diagnosis of a virus infection after the outcome of pregnancy was known, was allowed to affect the inclusion of a case in the analysis.

The eventual outcome of the pregnancies was recorded locally on Record Cards, the infants were medically examined at birth and at the age of one and two years, and any congenital defects found were recorded. Records were finally available for analysis of 578 pregnancies complicated by rubella, in 202 of which the rubella had occurred in the first twelve weeks of pregnancy. One hundred and three pregnancies complicated by measles, 298 by chickenpox, 501 by mumps, 33 by poliomyelitis and 166 by influenza were also analysed. The control series numbered 5,717. Twin births were excluded from the main analysis.

The main differences in outcome between the rubella and control series were that in pregnancies in which rubella occurred in the early months (virtually the first 12 weeks) there was a higher proportion of abortions and still births, a higher proportion of infants who failed to survive to their second birthday, a higher proportion of infants with congenital abnormalities, particularly those of the heart, eye and ear, and a higher proportion of infants of low birthweight.

The outcome of the pregnancies is summarized in the following table. (Because cases might be selected at any time during pregnancy, the controls were standardized for period under observation in order to achieve a better comparison of outcome).

	Abortions	Still births	Children dying under 2 years	Children alive at 2 years
Rubella up to 12th week	5.0	4.5	6.9	83.6
Control	2.4	2.4	2.4	92.8
Rubella after 12th week	0.3	3.0	2.7	94.0
Control	0.5	2.6	2.6	94.3

In fact, all the deaths of children in the rubella group occurred in the first year of life, and the infant mortality rate for the infants whose mothers had rubella in the first 12 weeks of pregnancy was 76.5 per thousand live births, compared with 25.8 per thousand in the controls. Amongst the children who died, 46 per cent of the rubella series had major congenital malformations, compared with 34 per cent of the controls, and nearly half of those born after the 36th week of pregnancy weighed 5½ lb. or less, compared with one-fifth of the controls.

At the medical examinations up to the age of two years, the following proportions of live born children were found to have major congenital malformations:

	All live-born infants	Infants surviving to 2 years
Control cases	$\frac{3}{2.3}$	$\frac{3}{1.3}$
Rubella up to 12th week ..	15.8	13.0
Rubella after 12th week ..	2.2	1.1

The chief types of defects found in the children surviving to 2 years were :

Type of defect	Control	Rubella up to 12th week	Rubella after 12th week
Congenital heart disease ..	$\frac{0.2}{0.2}$	$\frac{4.7}{4.7}$	$\frac{0.3}{0.3}$
Cataract	0.04	4.7	—
Deafness	0.08	3.0	—
Suspected deafness	0.4	3.6	0.8

All major congenital defects of these types occurred in children whose mothers had rubella up to the 12th week of pregnancy. A few cases of slight impairment of hearing, only discovered at later examinations (see below), occurred in children whose mothers had rubella in the 14th and 15th weeks.

Certain other defects appeared in a somewhat higher proportion in the surviving children whose mothers had rubella in the first 12 weeks of pregnancy. Mental defect was present in 1.8 per cent compared with 0.4 per cent of controls, and pyloric stenosis in 1.2 per cent compared with 0.2 per cent of controls. intestinal atresia, which appeared in 0.6 per cent of the rubella cases, did not occur at all in the control cases.

The live-born children whose mothers had rubella in the first twelve weeks of pregnancy also tended to have lower birth weights than the controls; 16.1 per cent of those delivered after the 36th week of pregnancy weighed 5½ lb. or less compared with 3.8 per cent of controls. This excess of small infants was observed not only in the infants with major congenital malformations but also in those without.

When the children covered by this enquiry reached the age of 3-5 years special examinations were carried out to determine whether there were cases of deafness of any other defect which had not been detected at the examinations up to two years. In the London and Middlesex areas children whose mothers had rubella in early pregnancy and a matched control group were examined by a standard technique. Several cases of previously undiagnosed impairment of hearing were found and so later examinations, of the rubella children only, were extended throughout the country.

From all these re-examinations it would appear that the incidence of impairment of hearing following rubella within the first 12 weeks of pregnancy is around 19 per cent. In only a small proportion of the affected children was deafness a severe handicap, some two-thirds of them were able to attend ordinary schools. No new defects other than deafness were found at these re-examinations.

There was nothing to suggest that any of the other virus infections, except possibly measles, occurring during pregnancy is followed by ill-effects to the foetus.

When chickenpox and mumps had occurred during pregnancy there was no evidence whatever of harmful effects to the child. In the measles series there was a somewhat higher infant death rate and also a higher proportion of malformed children than would be expected, but these findings provide no strong evidence that this outcome was due to the occurrence of measles during the pregnancies. The poor outcome of the cases complicated by poliomyelitis during pregnancy cannot be considered surprising in view of the severity of the disease itself. The children born to the group of mothers who had influenza in the second trimester of pregnancy showed a higher death rate by the age of two years than would be expected, but it is considered unlikely that this was due to the occurrence of influenza.

ACKNOWLEDGEMENTS

We are deeply indebted to many whose work has contributed to this report: to Dr. I. A. G. Macqueen (now Medical Officer of Health of Aberdeen) and Dr. P. L. McKinlay of the Department of Health for Scotland who organised the enquiry north of the border; to Dr. A. D. M. Jackson, Institute of Child Health, Great Ormond Street, and Dr. L. Fisch, Audiology Unit, Institute of Laryngology and Otology, Gray's Inn Road, who examined the London and Middlesex children and who have written Section 1 of Chapter V, and to Dr. J. A. Scott, County Medical Officer London, and Dr. A. C. T. Perkins, County Medical Officer, Middlesex, for making arrangements for these examinations; and, above all, to the medical officers of local health authorities in England, Wales and Scotland who carried out the essential field work.

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APPENDICES

Appendix 1. Tables.

- Table A. Distribution and percentage distribution of virus and control series according to:
- (a) Age of mother at confinement and
 - (b) Parity of mother.
- Table B. Distribution and percentage distribution of virus and control series according to place of confinement.
- Table C. Distribution and percentage distribution of virus and control series according to type of area of residence.
- Table D. Proportions of single and multiple deliveries in the virus and control series.
- Table E. Proportion of cases in each virus series in which infection was confirmed by a doctor, according to degree of severity of the infection.
- Table F. Proportions of control and virus series selected in each four-weekly period of pregnancy.
- Table G. Outcome to infant in pregnancies in each virus series according to the stage in pregnancy when the infection occurred, compared with the expected outcome calculated from the experience of standardized control groups.
- Table H. Numbers and proportions of infants delivered after the 36th week of pregnancy who were still born and who died under two years, in the control series and in each virus series according to the stage in pregnancy when infection occurred, for (a) infants without major malformations, (b) infants with major malformation, (c) all infants.
- Table K1. Numbers and proportion of infants delivered after the 36th week of pregnancy who weighed $5\frac{1}{2}$ lb. or less, in the control and rubella series, (distinguishing cases with rubella up to and after the 12th week of pregnancy), according to survival of infant and presence or absence of malformation.
- Table K2. Median birth weights of infants delivered at the 39th to 42nd weeks* of pregnancy, for the control, rubella, chickenpox and mumps series (distinguishing cases in which rubella occurred up to and after the 12th week of pregnancy).
- Table K3. Distribution and percentage distribution of birth weights of control infants and those in which rubella had occurred up to the 12th week and who were delivered at the 39th to 42nd weeks (live born infants only).

Table K4. Distribution and percentage distribution of birth weights of live born infants in the control and rubella series (distinguishing cases with rubella up to the 12th week of pregnancy) who were delivered at the 39th to 42nd weeks; infants with and without major malformation shown separately.

Table L. Numbers and proportions of infants with and without major malformation in the control series and in each virus series according to the stage in pregnancy when the infection occurred, for (a) all infants, (b) infants born dead, (c) all live-born infants, (d) infants born alive but dying under two years, (e) infants alive at two years (the table excludes cases delivered up to the 28th week of pregnancy).

Table M. Numbers and proportions of infants with and without major malformation in the control and rubella series according to parity of mother (rubella up to 12th week shown separately).

Table N. Numbers and proportions of infants with and without major malformation in the control and rubella series according to age of mother (rubella up to 12th week shown separately).

Appendix 2. Record Card.

Appendix 3. Rubella cases selected in certain areas in 1953.

Table A. Distribution and percentage distribution of virus and control series according to (a) Age of mother at confinement, and (b) Parity of mother

Type of case	(a) Age of Mother at Confinement (years)																All ages No.	%
	15-		20-		25-		30-		35-		40-		45 and over		Not known			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%		
Control series ..	276	5	1,641	28	1,901	33	1,201	21	594	10	165	3	8	0	22	0	5,808	100
Rubella ..	34	6	187	32	169	29	119	20	65	11	8	1	0	—	3	1	585	100
Measles ..	5	5	25	24	46	45	17	16	8	8	2	2	0	—	0	—	103	100
Chickenpox ..	19	6	91	30	104	34	58	20	24	8	3	1	0	—	4	1	303	100
Mumps ..	12	2	111	22	181	36	139	28	47	9	12	3	1	0	1	0	504	100
Poliomyelitis ..	2	6	13	40	10	30	6	18	1	3	1	3	0	—	0	—	33	100
Influenza ..	6	4	34	20	53	31	40	24	29	17	6	4	0	—	0	—	168	100

Type of case	(b) Parity of Mother (number of previous pregnancies)															Not stated No.	%	All parities No.	%			
	0		1		2		3		4		5		6		7					8 or more		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.					%	No.	%
Control series ..	2,097	36	1,689	29	991	17	475	8	252	5	118	2	70	1	37	1	72	1	7	0	5,808	100
Rubella...	192	33	134	23	126	22	67	11	41	7	14	2	4	1	1	0	5	1	1	0	585	100
Measles...	35	34	26	25	20	19	14	14	8	8	0	—	0	—	0	—	0	—	0	—	103	100
Chickenpox ..	102	34	83	28	64	21	41	14	7	2	3	1	1	0	0	—	1	0	1	0	303	100
Mumps...	124	25	137	27	136	27	61	12	26	5	8	2	5	1	2	0	5	1	0	—	504	100
Poliomyelitis ..	9	27	8	24	11	34	3	9	2	6	0	—	0	—	0	—	0	—	0	—	33	100
Influenza ..	45	27	35	21	34	20	21	13	14	8	6	4	4	2	2	1	7	4	0	—	168	100

Table B. Distribution and percentage distribution of virus and control series according to place of confinement

Type of case	Place of Confinement						All cases
	Home		Institution		Not known		
	No.	%	No.	%	No.	%	
Control	2,011	35	3,797	65	0	—	5,808
Rubella	209	36	375	64	1	0	585
Measles	31	30	71	69	1	1	103
Chickenpox	94	31	209	69	0	—	303
Mumps	203	40	301	60	0	—	504
Poliomyelitis	5	15	28	85	0	—	33
Influenza	78	46	90	54	0	—	168

Table C. Distribution and percentage distribution of virus and control series according to type of area of residence

Type of case	Type of Area of Residence								All cases
	Urban				Rural				
	England and Wales No. %		Scotland No. %		England and Wales No. %		Scotland No. %		
Control	4,849	83	450	8	479	8	30	1	5,808
Rubella	466	80	17	3	97	16	5	1	585
Measles	73	71	1	1	26	25	3	3	103
Chickenpox ..	253	83	11	4	35	12	4	1	303
Mumps	399	79	16	3	83	17	6	1	504
Poliomyelitis ..	25	76	0	—	7	21	1	3	33
Influenza ..	168	100	—	—	—	—	—	—	168

Table D. Proportions of single and multiple deliveries in the virus and control series.

Type of case	Single births		Twins		Triplets		Total
	No.	%	No.	%	No.	%	
Control	5,717	98.4	91	1.6	Nil		5,808
Rubella—Total	578	98.8	7	1.2			585
Up to 16th week	277	99.3	2	0.7			279
17th to 28th weeks	201	98.0	4	2.0			205
After 28th week	96	99.0	1	1.0			97
Date of onset not stated	4	—	0	—			4
Measles	103	100.0	0	—			103
Chickenpox	298	98.3	5	1.7			303
Mumps	501	99.4	3	0.6			504
Poliomyelitis	33	100.0	0	—			33
Influenza	166	98.8	2	1.2			168

Table E. Proportion of cases in each virus series in which infection was confirmed by a doctor, according to degree of severity of the infection

Type of case			Degree of Severity		Confirmed by a Doctor		Not confirmed by a Doctor		All cases
					No.	%	No.	%	
Rubella	Mild	269	95	15	5	284	
			Moderate	195	99	2	1	197	
			Severe	36	97	1	3	37	
			Not stated	15	22	52	78	67	
			All cases	515	88	70	12	585	
Measles	Mild	25	89	3	11	28	
			Moderate	39	100	0	—	39	
			Severe	19	90	2	10	21	
			Not stated	2	13	13	87	15	
			All cases	85	83	18	17	103	
Chickenpox	Mild	86	95	5	5	91	
			Moderate	130	97	4	3	134	
			Severe	40	95	2	5	42	
			Not stated	6	17	30	83	36	
			All cases	262	86	41	14	303	
Mumps	Mild	175	93	14	7	189	
			Moderate	185	98	4	2	189	
			Severe	60	92	5	8	65	
			Not stated	12	20	49	80	61	
			All cases	432	86	72	14	504	
Poliomyelitis	Mild	12	100	0	—	12	
			Moderate	11	100	0	—	11	
			Severe	3	—	1	—	4	
			Not stated	3	50	3	50	6	
			All cases	29	88	4	12	33	
Influenza	Mild	27	63	16	37	43	
			Moderate	30	64	17	36	47	
			Severe	27	79	7	21	34	
			Not stated	13	30	31	70	44	
			All cases	97	58	71	42	168	

Table F. Proportions of control and virus series selected in each four-weekly period of pregnancy

Time in pregnancy when selected (weeks)		Type of case											
		Control		Rubella		Measles		Chickenpox		Mumps		Polionyelitis	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Up to 8th	90	2	4	1	0	—	5	2	2	—	0	—
—12th	819	14	34	6	9	9	9	3	20	4	2	6
—16th	1,214	21	67	12	7	7	25	8	54	11	4	12
—20th	1,085	19	88	15	14	14	39	13	56	11	2	6
—24th	843	15	93	16	14	14	38	13	64	13	11	34
—28th	691	12	89	15	16	15	56	19	64	13	6	18
Total up to 28th	4,742	83	375	65	60	59	172	58	260	52	25	76
—32nd	460	8	91	16	17	16	36	12	87	18	6	18
—36th	335	6	62	11	18	17	55	18	96	19	0	—
Total 29th to 36th	795	14	153	27	35	33	91	30	183	37	6	18
—40th	170	3	49	8	7	7	33	11	51	10	2	6
after 40th	10	—	1	—	1	1	2	1	7	1	0	—
Total after 36th	180	3	50	8	8	8	35	12	58	11	2	6
All cases	5,717	100	578	100	103	100	298	100	501	100	33	100
												166	100

Table G. Outcome to infant in pregnancies in each virus series according to the stage in pregnancy when the infection occurred, compared with the expected outcome calculated from the experience of standardized control groups

RUBELLA										MEASLES									
Stage of Pregnancy at which Rubella occurred	No. of cases	Outcome to Infant						Stage of Pregnancy at which Measles occurred	No. of cases	Outcome to Infant									
		Abortion	Still birth	Born alive, but died under 2 years	Alive at 2 years	Abortion	Still birth			Born alive, but died under 2 years	Alive at 2 years								
		No.	%	No.	%	No.	%			No.	%	No.	%	No.	%	No.	%		
Up to 4th week ..	51	3	5.9	3	5.9	4	7.8	41	80.4	Up to 4th week ..	9	0	0	0	0	7	77.8		
5th to 8th weeks ..	69	2	2.9	1.3	2.3	1.3	2.3	47.3	92.8	5th to 8th weeks ..	15	1	6.7	2	13.3	11	73.8		
9th to 12th weeks ..	82	2	2.9	1.9	2.8	1.6	2.3	63.6	92.1	9th to 12th weeks ..	13	0	0	0	0	13	91.9		
13th to 16th weeks ..	75	5	6.1	0	—	3	6.1	72	87.8	13th to 16th weeks ..	9	0	0	0	0	11	84.6		
Total up to 12th week	202	1.9	2.3	1.6	2.0	2.0	2.4	76.5	93.3	Total up to 12th week	37	0.2	0.5	0.3	0.8	12	32.4		
17th to 20th weeks ..	79	10	5.0	9	4.5	14	6.9	189	83.6	17th to 20th weeks ..	13	1	7.7	1	7.7	20	78.4		
21st to 24th weeks ..	68	4.9	2.4	4.8	4.9	2.4	187.4	92.8	21st to 24th weeks ..	15	0.7	1.0	0.9	2.4	34.4	93.0			
25th to 28th weeks ..	34	1	1.3	2	2.7	2	2.7	70	93.3	25th to 28th weeks ..	9	1	11.1	0	0	8	88.9		
Total 13th to 24th weeks	276	1.0	1.3	2.1	2.6	2.0	2.7	69.9	93.2	Total 13th to 24th weeks	46	0.1	0.3	0.2	0.5	44	95.6		
29th to 32nd weeks ..	50	0	—	1	1.5	4	5.9	63	92.6	29th to 32nd weeks ..	9	0	0	0	0	9	100.0		
33rd to 36th weeks ..	31	0	—	2	3.7	1	1.9	31	94.4	33rd to 36th weeks ..	9	0	0	0	0	8	88.9		
37th week or over ..	15	0	—	1	1.5	2	2.7	15	94.4	37th week or over ..	2	0	0	0	0	2	100.0		
Total 29th week or over	96	0	—	0	—	0	—	96	100.0	Total 29th week or over	20	0	0	0	0	19	95.0		
Week of onset N.S. ...	4	0	—	0	—	0	—	4	100.0	Week of onset N.S. ...	0	0	0	0	0	0	0		
All Rubella cases ..	578	11	1.9	20	3.5	24	4.2	523	90.4	All Measles cases ..	103	2	1.9	2	1.9	8	7.8		
		6.9	1.2	14.6	2.5	14.6	2.5	541.9	93.8			1.0	1.0	2.3	2.3	96.8	94.0		

Table G (contd.)

CHICKENPOX				MUMPS							
Stage of Pregnancy at which Chickenpox occurred	No. of cases	Outcomes to Infant				Stages of Pregnancy at which Mumps occurred	No. of cases	Outcomes to Infant			
		Abortion	Still birth	Born alive, but died under 2 years	Alive at 2 years			Abortion	Still birth	Born alive, but died under 2 years	Alive at 2 years
No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Up to 4th week ..	20	Observed Expected 1 5.0 0.6 3.0	0 0 0 0.6	1 5.0 1 5.0	18 90.0 18.4 92.0	Up to 4th week ..	20	Observed Expected 1 5.0 0.5 2.5	0 0 0 0.5	0 0 0 0.5	19 95.0 18.5 92.5
5th to 8th weeks ..	32	Observed Expected 1 3.1 0 0	2 6.3 0 0	1 3.1 0 0	28 87.5 29.6 92.5	8th to 8th weeks ..	34	Observed Expected 0 0 0 0	2 5.9 0 0	0 0 0 0	32 94.1 31.6 92.9
9th to 12th weeks ..	24	Observed Expected 1 4.2 0 0	1 4.2 0 0	0 0 0 0	22 91.6 22.3 92.9	9th to 12th weeks ..	65	Observed Expected 3 4.6 1.4 2.2	3 4.6 1.8 2.8	1 1.5 1.6 2.5	61 93.9 60.2 92.5
Total up to 12th week	76	Observed Expected 3 3.9 1.8 2.4	3 3.9 2.1 2.8	2 2.6 2.4 3.2	68 89.6 70.3 92.4	Total up to 12th week	119	Observed Expected 4 3.4 2.6 2.2	2 1.7 3.2 2.7	1 0.8 2.4 2.0	112 94.1 110.3 92.7
13th to 16th weeks ..	28	Observed Expected 1 3.6 0 0	0 0 0 0	0 0 0 0	27 96.4 26.2 93.5	13th to 16th weeks ..	55	Observed Expected 0 0 0 0	1 1.8 1.5 2.7	0 0 1.4 2.5	54 98.2 51.3 93.3
17th to 20th weeks ..	39	Observed Expected 0 0 0 0	0 0 0 0	2 5.1 2.6 6.7	37 94.9 35.6 93.8	17th to 20th weeks ..	51	Observed Expected 1 2.0 0.4 0.8	2 3.9 1.4 2.7	2 3.9 1.3 2.5	46 90.2 47.9 94.0
21st to 24th weeks ..	36	Observed Expected 0 0 0 0	1 2.8 1.0 2.8	1 2.8 1.0 2.8	34 94.4 33.9 94.1	21st to 24th weeks ..	69	Observed Expected 0 0 0 0	2 2.9 1.9 2.8	3 4.3 1.8 2.6	64 92.8 63.1 94.3
25th to 28th weeks ..	41	Observed Expected 0 0 0 0	1 2.4 1.1 2.7	1 2.4 1.1 2.7	39 95.2 38.8 94.6	25th to 28th weeks ..	56	Observed Expected 0 0 0 0	1 1.8 1.5 2.7	2 3.6 1.5 2.7	53 94.6 53.0 94.6
Total 13th to 28th weeks	144	Observed Expected 1 0.7 0.5 0.4	2 1.4 2 2.8	4 2.8 3.8 2.6	137 95.1 135.5 94.1	Total 13th to 28th weeks	231	Observed Expected 1 0.4 1.4 0.6	6 2.6 6.3 2.7	7 3.0 6.0 2.6	217 93.9 217.3 94.1
29th to 32nd weeks ..	37	Observed Expected 0 0 0 0	0 0 0 0	0 0 0 0	37 100.0 35.2 95.2	29th to 32nd weeks ..	68	Observed Expected 0 0 0 0	0 0 0 0	1 1.5 1.6 2.4	67 98.5 64.7 95.1
33rd to 36th weeks ..	26	Observed Expected 0 0 0 0	0 0 0 0	1 3.8 0.6 2.3	25 96.2 24.9 95.4	33rd to 36th weeks ..	60	Observed Expected 0 0 0 0	0 0 0 0	2 3.3 1.3 2.2	58 96.7 57.5 95.8
37th week or over ..	14	Observed Expected 0 0 0 0	0 0 0 0	1 7.1 0.3 2.1	13 92.9 13.5 96.5	37th week or over ..	19	Observed Expected 0 0 0 0	1 5.3 0.4 2.1	1 5.3 0.4 2.1	17 89.4 18.3 96.3
Total 29th week or over	77	Observed Expected 0 0 0 0	0 0 0 0	2 2.6 1.8 2.5	75 97.4 73.5 95.5	Total 29th week or over	147	Observed Expected 0 0 0 0	1 0.7 3.2 2.2	4 2.7 3.3 2.2	142 96.6 140.8 95.6
Week of onset N.S. ...	1	Observed Expected 0 0 0 0	0 0 0 0	0 0 0 0	1 100.0 1.0 100.0	Week of onset N.S. ...	4	Observed Expected 0 0 0 0	0 0 0 0	0 0 0 0	4 100.0 4 100.0
All Chickenpox cases	208	Observed Expected 4 1.9 2.5 0.8	5 2.4 7.8 2.6	8 3.8 7.4 2.5	201 96.6 200.3 94.1	All Mumps cases ..	501	Observed Expected 5 1.0 4 0.8	9 1.8 12.8 2.6	12 2.4 12.3 2.5	478 94.8 471.9 94.1

Table G (contd.)

POLIO-MYELITIS

INFLUENZA

Stage of Pregnancy at which Poliomyelitis occurred	No. of cases	Outcome to Infant				Stage of Pregnancy at which Influenza occurred	No. of cases	Outcome to Infant				Abortion	Still birth		Born alive, but died under 2 years	Alive at 2 years
		Observed	Expected	No.	%			Observed	Expected	No.	%		No.	%		
Up to 4th week	1	Observed	Expected	0	—	Up to 4th week	5	Observed	Expected	0	—	0	0	—	0	5
5th to 8th weeks	2	Observed	Expected	0	—	5th to 8th weeks	21	Observed	Expected	0	—	4.0	0.1	2.0	0	4.6
9th to 12th weeks	6	Observed	Expected	0	—	9th to 12th weeks	16	Observed	Expected	0	—	4.8	0	2.9	1	19
Total up to 12th week	9	Observed	Expected	1	16.7	Total up to 12th week	42	Observed	Expected	0	—	9.6	0	5.8	0.5	19.3
13th to 16th weeks	10	Observed	Expected	2	22.2	13th to 16th weeks	22	Observed	Expected	0	—	3.3	0	3.1	0	16
17th to 20th weeks	7	Observed	Expected	1	14.3	17th to 20th weeks	28	Observed	Expected	1	2.4	2.6	0	2.9	1	40
21st to 24th weeks	7	Observed	Expected	2	28.6	21st to 24th weeks	26	Observed	Expected	0	—	0.3	0	0.3	0	25.3
25th to 28th weeks	0	Observed	Expected	0	—	25th to 28th weeks	23	Observed	Expected	0	—	0.7	0	0.7	0	26.3
Total 13th to 28th weeks	24	Observed	Expected	0	—	Total 13th to 28th weeks	99	Observed	Expected	0	—	0.8	0	0.8	0	27
29th to 32nd weeks	0	Observed	Expected	0	—	29th to 32nd weeks	14	Observed	Expected	0	—	0.5	0	0.5	0	25.3
33rd to 36th weeks	0	Observed	Expected	0	—	33rd to 36th weeks	8	Observed	Expected	0	—	0.4	0	0.4	0	24.5
37th week or over	0	Observed	Expected	0	—	37th week or over	3	Observed	Expected	0	—	0.1	0	0.1	0	24.5
Total 29th week or over	0	Observed	Expected	0	—	Total 29th week or over	25	Observed	Expected	0	—	0.1	0	0.1	0	2.9
Week of onset N.S.	0	Observed	Expected	0	—	Week of onset N.S.	0	Observed	Expected	0	—	0	0	0	0	—
All Poliomyelitis cases	33	Observed	Expected	1	3.0	All Influenza cases	146	Observed	Expected	1	0.6	1.6	2	1.2	6	157
				0.4	1.2								4.5	2.9		158.7

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Table H. Numbers and proportions of infants delivered after the 36th week of pregnancy who were still born and who died under two years, in the control series and in each virus series according to the stage in pregnancy when infection occurred, for (a) infants without major malformation, (b) infants with major malformation, (c) all infants

MEASLES						
Type of case	No. of cases	Still born		Died under 2 years old		
		No.	%	No.	%	
(a) Infants without major malformation						
Control series	5,109	68	1.3	69	1.4	
Measles at up to 12th week ..		30	0	2	6.7	
Measles at 13th to 28th weeks ..		42	0	0	0	
Measles at 29th to 40th weeks ..		19	0	1	5.3	
All measles cases		91	0	3	3.3	
(b) Infants with major malformation						
Control series	134	20	14.9	39	29.1	
Measles at up to 12th week ..		4	0	3	—	
Measles at 13th to 28th weeks ..		3	1	0	—	
Measles at 29th to 40th weeks ..		1	0	1	—	
All measles cases		8	1	4	50.0	
(c) All infants						
Control series	5,243	88	1.7	108	2.1	
Measles at up to 12th week ..		34	0	5	14.7	
Measles at 13th to 28th weeks ..		45	1	0	0	
Measles at 29th to 40th weeks ..		20	0	2	10.0	
All measles cases		99	1	7	7.1	

RUBELLA						
Type of case	No. of cases	Still born		Died under 2 years old		
		No.	%	No.	%	
(a) Infants without major malformation						
Control series	5,109	68	1.3	69	1.4	
Rubella at up to 12th week ..		152	5	5	3.3	
Rubella at 13th to 28th weeks ..		260	5	5	1.9	
Rubella at 29th to 40th weeks ..		90	0	1	1.1	
All rubella cases		506*	10	11	2.2	
(b) Infants with major malformation						
Control series	134	20	14.9	39	29.1	
Rubella at up to 12th week ..		29	2	7	24.1	
Rubella at 13th to 28th weeks ..		7	2	2	28.6	
Rubella at 29th to 40th weeks ..		1	1	0	—	
All rubella cases		37	5	9	24.3	
(c) All infants						
Control series	5,243	88	1.7	108	2.1	
Rubella at up to 12th week ..		181	7	12	6.6	
Rubella at 13th to 28th weeks ..		267	7	7	2.6	
Rubella at 29th to 40th weeks ..		91	1	1	1.1	
All rubella cases		543*	15	20	3.7	

* Includes 4 cases where the date of onset of rubella was not known, all alive at 2 years.

(Table continued overleaf)

Table H (contd.)

CHICKENPOX				MUMPS			
Type of case	No. of cases	Still born	Died under 2 years old	Type of case	No. of cases	Still born	Died under 2 years old
	No.	%	No.		No.	%	No.
(a) Infants without major malformation				(a) Infants without major malformation			
Control series	5,109	68	1.3	69	1.4	68	1.3
Chickenpox at up to 12th week ..	70	1	1.4	2	2.9	1	0.9
Chickenpox at 13th to 28th weeks ..	136	0	0	0	0	0	0
Chickenpox at 29th to 40th weeks ..	73	0	0	1	1.4	0	0
All chickenpox cases	280*	1	0.4	3	1.1	0	0
(b) Infants with major malformation				(b) Infants with major malformation			
Control series	134	20	14.9	39	29.1	20	14.9
Chickenpox at up to 12th week ..	1	0	—	0	—	0	—
Chickenpox at 13th to 28th weeks ..	2	0	—	2	—	1	14.3
Chickenpox at 29th to 40th weeks ..	2	0	—	1	—	0	—
All chickenpox cases	5	0	0	3	60.0	1	8.3
(c) All infants				(c) All infants			
Control series	5,243	88	1.7	108	2.1	88	1.7
Chickenpox at up to 12th week ..	71	1	1.4	2	2.8	1	0.9
Chickenpox at 13th to 28th weeks ..	138	0	0	2	1.4	1	0.5
Chickenpox at 29th to 40th weeks ..	75	0	0	2	2.7	0	0
All chickenpox cases	285*	1	0.4	6	2.1	2	0.4

* Includes 1 case where date of onset of chickenpox was not known, alive at 2 years.

* Includes 4 cases where the date of onset of mumps was not known, all alive at 2 years.

Table H (contd.)

POLIOMYELITIS					INFLUENZA				
Type of case		No. of cases	Still born	Died under 2 years old	Type of case		No. of cases	Still born	Died under 2 years old
		No.	%	No. %			No.	%	No. %
(a) Infants without major malformation					(a) Infants without major malformation				
Control series	..	5,109	68	1.3	69	1.4	5,109	68	1.3
Poliomyelitis at up to 12th week	..	4	0	—	0	0	40	0	1
Poliomyelitis at 13th to 28th weeks	..	24	0	0	1	4.2	90	1	3
Poliomyelitis at 29th to 40th weeks	..	0	0	—	0	—	25	0	0
All poliomyelitis cases	..	28	0	0	1	3.6	155	1	0.6
(b) Infants with major malformation					(b) Infants with major malformation				
Control series	..	134	20	14.9	39	29.1	134	20	14.9
Poliomyelitis at up to 12th week	..	0	0	—	0	—	0	0	0
Poliomyelitis at 13th to 28th weeks	..	0	0	—	0	—	7	1	14.3
Poliomyelitis at 29th to 40th weeks	..	0	0	—	0	—	0	0	—
All poliomyelitis cases	..	0	0	—	0	—	7	1	14.3
(c) All infants					(c) All infants				
Control series	..	5,243	88	1.7	108	2.1	5,243	88	1.7
Poliomyelitis at up to 12th week	..	4	0	—	0	—	40	0	1
Poliomyelitis at 13th to 28th weeks	..	24	0	0	1	4.2	97	2	2.1
Poliomyelitis at 29th to 40th weeks	..	0	0	—	0	—	25	0	0
All poliomyelitis cases	..	28	0	0	1	3.6	162	2	1.2

Table K1. Numbers and proportion of infants delivered after the 36th week of pregnancy who weighed 5½ lb. or less, in the control and rubella series, (distinguishing cases with rubella up to and after the 12th week of pregnancy), according to survival of infant and presence or absence of malformation

Type of case	Still births		Deaths under 2 years old		Infants alive at 2 years		All infants	
	No. of cases	Underweight (5½ lb. or less) No.	No. of cases	Underweight (5½ lb. or less) No.	No. of cases	Underweight (5½ lb. or less) No.	No. of cases	Underweight (5½ lb. or less) No.
<i>(a) Infants without major malformation</i>								
Control series	68	15	69	13	4,972	166	5,109	194
Rubella up to 12th week ..	5	4	5	2	142	13	152	19
Rubella after 12th week ..	5	0	6	1	339	14	350	15
All rubella cases	10	4	11	3	485*	28*	506*	35*
<i>(b) Infants with major malformation</i>								
Control series	20	11	39	8	75	10	134	29
Rubella up to 12th week ..	2	0	7	6	20	7	29	13
Rubella after 12th week ..	3	0	2	0	3	0	8	0
All rubella cases	5	0	9	6	23	7	37	13
<i>(c) All Infants</i>								
Control series	88	26	108	21	5,047	176	5,243	223
Rubella up to 12th week ..	7	4	12	8	162	20	181	32
Rubella after 12th week ..	8	0	8	1	342	14	358	15
All rubella cases	15	4	20	9	508*	35*	543*	48*

* Includes 4 cases where the date of onset of rubella was not known, of whom one was underweight.

Table K2. Median birth weights of live born infants delivered at the 39th to 42nd weeks of pregnancy, for the control, rubella, chickenpox and mumps series (distinguishing cases in which rubella occurred up to and after the 12th week of pregnancy)

Type of case	Week in which delivered												
	39th			40th		41st		42nd		Total, 39th to 42nd			
	No. of cases	Median birth-weight	lb. oz.	No. of cases	Median birth-weight	lb. oz.	No. of cases	Median birth-weight	lb. oz.	No. of cases	Median birth-weight		
Control	578	7 0	1,325	7 4	1,427	7 8	864	7 12	4,194	7 6
Rubella up to 12th week	17	6 10	40	7 8	50	7 0	32	7 5	139	7 1
Rubella after 12th week	39	7 3	85	7 6	110	7 9	53	7 8	287	7 8
Chickenpox	26	7 3	80	7 4	67	7 10	53	8 0	226	7 8
Mumps	48	7 6	115	7 6	122	7 12	93	8 0	378	7 8

Table K3. *Distribution and percentage distribution of birth weights of control infants and those in which rubella had occurred up to the 12th week and who were delivered at the 39th to 42nd weeks (liveborn infants only)*

Week in which delivered	Type of case	Birth weight																				All birth weights		
		3 lb.-		4 lb.-		5 lb.-		6 lb.-		7 lb.-		8 lb.-		9 lb.-		10 lb.-		11 lb.-		12 lb. and over			Not stated No.	%
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%			
39th	Control	1	0.2	6	1.0	61	10.5	308	33.9	183	31.6	96	16.9	20	3.5	1	0.2	—	—	—	—	1	0.2	539
	Rubella up to 12th week	—	—	2	11.8	2	11.8	6	33.3	4	23.5	3	17.6	—	—	—	—	—	—	—	—	—	—	17
40th	Control	1	0.1	5	0.4	94	7.1	359	26.4	503	37.8	282	21.2	65	4.9	24	1.8	—	—	1	0.1	3	0.2	1,323
	Rubella up to 12th week	—	—	1	2.5	4	10.0	8	20.0	17	42.5	9	22.5	1	2.5	—	—	—	—	—	—	—	—	40
41st	Control	2	0.1	4	0.3	67	4.7	284	19.9	568	39.8	358	25.0	115	8.0	27	1.9	2	0.1	—	—	3	0.2	1,430
	Rubella up to 12th week	1	2.0	6	12.0	4	8.0	13	26.0	20	40.0	3	6.0	2	4.0	1	2.0	—	—	—	—	—	—	50
42nd	Control	—	—	1	0.1	29	3.4	155	17.9	304	35.1	353	29.2	100	11.6	20	2.3	2	0.2	—	—	1	0.1	865
	Rubella up to 12th week	—	—	2	6.2	3	9.4	7	21.9	12	37.5	6	18.8	2	6.2	—	—	—	—	—	—	—	—	32

Table K4. Distribution and percentage distribution of birth weights of live born infants in the control and rubella series (distinguishing cases with rubella up to the 12th week of pregnancy) who were delivered at the 39th to 42nd weeks), infants with and without major malformations shown separately

Week in which delivered	Type of case	Infants with major malformation						Infants without major malformation															
		Birth-weight						All birth-weights	Birth-weight														
		-34 lb. No.	-34 lb. %	-7 lb. No.	-7 lb. %	over 7 lb. No.	over 7 lb. %		N.S. No.	N.S. %													
36th	Control	0	—	3	18	7	41	7	41	0	0	17	0	—	29	5	268	48	264	47	1	2	562
	Rubella up to 12th week	0	—	2	—	2	—	0	—	0	—	4	0	—	1	8	5	38	7	54	0	—	13
	Rubella after 12th week	0	—	0	—	1	—	0	—	0	—	1	0	—	1	3	17	45	20	53	0	—	38
40th	Control	0	—	4	15	11	41	12	44	0	—	27	1	1	33	2-5	487	37	377	50	3	2	1,301
	Rubella up to 12th week	0	—	2	29	2	29	3	42	0	—	7	0	—	3	9	8	34	22	67	0	—	33
	Rubella after 12th week	0	—	0	—	1	—	0	—	0	—	1	0	—	5	6	25	30	54	64	0	—	84
41st	Control	0	—	3	7	8	38	17	58	2	7	29	0	—	23	2	400	29	977	69	1	1	1,404
	Rubella up to 12th week	0	—	5	71	2	29	0	—	0	—	7	0	—	5	12	16	37	22	51	0	—	43
	Rubella after 12th week	0	—	0	—	2	—	0	—	0	—	2	0	—	1	1	28	26	79	73	0	—	100
42nd	Control	0	—	1	7	7	50	6	43	0	—	14	0	—	13	2	200	24	637	74	1	1	851
	Rubella up to 12th week	0	—	1	20	3	60	1	20	0	—	5	0	—	1	4	7	26	19	70	0	—	27
	Rubella after 12th week	0	—	0	—	0	—	0	—	0	—	0	0	—	1	2	16	50	36	68	0	—	53
39th to 42nd	Control	0	—	10	11	33	38	42	49	2	2	87	1	0	58	2	1,355	33	2,655	65	6	1	4,115
	Rubella up to 12th week	0	—	10	43	9	40	4	17	0	—	23	0	—	10	9	36	31	70	60	0	—	116
	Rubella after 12th week	0	—	0	—	4	—	0	—	0	—	4	0	—	8	3	86	30	189	67	0	—	283

Table L. Numbers and proportions of infants with and without major malformation in the control series and in each virus series according to the stage in pregnancy when the infection occurred, for (a) all infants, (b) infants born dead, (c) all live-born infants, (d) infants born alive but dying under two years, (e) infants alive at two years (the table excludes cases delivered up to the date week of pregnancy)

(c) ALL INFANTS														
Type of case	No. of cases	Infants without major malformation		Infants with major malformation		Not stated	(b) INFANTS BORN DEAD							
		No.	%	No.	%		No.	%	No.	%				
Control series	..	5,611	96.8	156	2.8	24	0.4	156	100	67.4	38	17.9	23	14.7
Rubella up to 4th week	..	48	40	83.3	8	16.7	0	2	2	66.7	1	0	0	33.3
Rubella 4th to 8th week	..	67	55	79.1	12	17.9	2	6	4	66.7	0	0	0	0
Rubella 8th to 12th week	..	77	67	87.0	10	13.0	0	9	6	66.7	1	11.1	2	22.2
Rubella up to 12th week	..	192	160	83.4	30	15.6	2	1	1	—	0	0	0	0
Rubella 12th to 16th week	..	74	71	95.9	3	4.1	0	2	2	—	0	0	0	0
Rubella 16th to 20th week	..	79	76	96.2	3	3.8	0	2	1	0	0	0	0	0
Rubella 20th to 24th week	..	68	65	95.6	3	4.4	0	2	1	0	0	0	0	0
Rubella 24th to 28th week	..	54	54	100.0	0	0	0	2	2	—	0	0	0	0
Rubella at 13th to 28th weeks	..	275	266	96.7	9	3.3	0	2	3	71.4	2	28.6	0	0
Rubella 32nd to 36th week	..	50	49	98.0	1	2.0	0	3	3	—	0	0	0	0
Rubella 36th to 40th week	..	31	31	100.0	0	0	0	0	0	0	0	0	0	0
Rubella 40th to 44th week	..	15	14	93.3	1	6.7	0	4	3	0	1	0	0	0
Rubella at 29th to 40th weeks	..	96	94	97.9	2	2.1	0	0	0	0	0	0	0	0
Rubella, date of onset N.S.	..	4	4	—	0	—	0	0	0	0	0	0	0	0
All Rubella cases	..	567	524	92.4	43	7.6	2	20	14	70.0	4	20.0	2	10.0
(c) INFANTS BORN ALIVE BUT DYING UNDER 2 YEARS														
Control series	..	140	92	65.7	47	33.6	1	5,315	3,334	98.5	81	1.5	0	—
Rubella up to 4th week	..	4	1	25.0	3	75.0	0	41	37	90.2	4	9.8	0	—
Rubella 4th to 8th week	..	5	2	40.0	3	60.0	0	56	47	83.9	9	16.1	0	—
Rubella 8th to 12th week	..	14	7	50.0	7	50.0	0	72	63	87.5	9	12.5	0	—
Rubella up to 12th week	..	19	11	57.9	8	42.1	0	169	147	87.0	22	13.0	0	—
Rubella 12th to 16th week	..	7	1	14.3	6	85.7	0	70	68	97.1	2	2.9	0	—
Rubella 16th to 20th week	..	4	2	50.0	2	50.0	0	75	74	98.7	1	1.3	0	—
Rubella 20th to 24th week	..	1	1	100.0	0	0	0	63	63	100.0	0	0	0	—
Rubella 24th to 28th weeks	..	5	5	100.0	0	0	0	51	51	100.0	0	0	0	—
Rubella at 13th to 28th weeks	..	19	11	57.9	8	42.1	0	259	256	98.8	3	1.2	0	—
Rubella 32nd to 36th week	..	0	0	—	0	—	0	47	46	97.9	1	2.1	0	—
Rubella 36th to 40th week	..	1	1	100.0	0	0	0	30	30	100.0	0	0	0	—
Rubella 40th to 44th week	..	0	0	—	0	—	0	14	14	100.0	0	0	0	—
Rubella at 29th to 40th weeks	..	1	1	100.0	0	0	0	91	90	98.9	1	1.1	0	—
Rubella, date of onset N.S.	..	0	0	—	0	—	0	4	4	—	0	0	0	—
All Rubella cases	..	26	13	54.2	11	45.8	0	533	497	95.0	26	5.0	0	—
(c) INFANTS ALIVE AT 2 YEARS														
Control series	..	5,435	5,326	97.6	128	2.3	1	5,435	5,326	97.6	128	2.3	1	0.0
Rubella up to 4th week	..	45	38	84.4	7	15.6	0	45	38	84.4	7	15.6	0	—
Rubella 4th to 8th week	..	61	49	80.3	12	19.7	0	61	49	80.3	12	19.7	0	—
Rubella 8th to 12th week	..	77	67	87.0	10	13.0	0	77	67	87.0	10	13.0	0	—
Rubella up to 12th week	..	183	154	84.2	29	15.8	0	183	154	84.2	29	15.8	0	—
Rubella 12th to 16th week	..	72	69	95.8	3	4.2	0	72	69	95.8	3	4.2	0	—
Rubella 16th to 20th week	..	77	75	97.4	2	2.6	0	77	75	97.4	2	2.6	0	—
Rubella 20th to 24th week	..	67	65	97.0	2	3.0	0	67	65	97.0	2	3.0	0	—
Rubella 24th to 28th weeks	..	52	52	100.0	0	0	0	52	52	100.0	0	0	0	—
Rubella at 13th to 28th weeks	..	268	261	97.4	7	2.6	0	268	261	97.4	7	2.6	0	—
Rubella 32nd to 36th week	..	47	46	97.9	1	2.1	0	47	46	97.9	1	2.1	0	—
Rubella 36th to 40th week	..	31	31	100.0	0	0	0	31	31	100.0	0	0	0	—
Rubella 40th to 44th week	..	14	14	100.0	0	0	0	14	14	100.0	0	0	0	—
Rubella at 29th to 40th weeks	..	92	91	98.9	1	1.1	0	92	91	98.9	1	1.1	0	—
Rubella, date of onset N.S.	..	4	4	—	0	—	0	4	4	—	0	—	0	—
All Rubella cases	..	547	510	95.2	37	6.8	0	547	510	95.2	37	6.8	0	—

Table L (contd.)

(a) ALL INFANTS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases
Control series	5,611	5,431	96.8	156	2.8	24	0.4
Measles up to 4th week	9	8	88.9	1	11.1	0	0
Measles - 4th week	14	11	78.6	3	21.4	0	0
Measles - 8th week	13	12	92.3	1	7.7	0	0
Measles up to 12th week	36	31	86.1	5	13.9	0	0
Measles - 16th week	8	7	87.5	1	12.5	0	0
Measles - 20th week	13	12	92.3	1	7.7	0	0
Measles - 24th week	15	15	100.0	0	0	0	0
Measles - 28th week	8	8	100.0	0	0	0	0
Measles at 18th to 28th weeks	45	42	93.3	3	6.7	0	0
Measles - 32nd week	9	9	100.0	0	0	0	0
Measles - 36th week	9	8	88.9	1	11.1	0	0
Measles - 40th week	2	2	100.0	0	0	0	0
Measles at 28th to 40th weeks	30	29	96.7	1	3.3	0	0
Measles, date of onset N.S.	0	0	0	0	0	0	0
All Measles cases	101	92	91.1	8	7.9	1	1.0

(b) INFANTS BORN ALIVE BUT DYING UNDER 2 YEARS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases
Control series	140	92	65.7	47	33.6	1	0.7
Measles up to 4th week	2	1	50.0	1	50.0	0	0
Measles - 4th week	2	1	50.0	1	50.0	0	0
Measles - 8th week	2	1	50.0	1	50.0	0	0
Measles up to 12th week	6	3	50.0	3	50.0	0	0
Measles - 16th week	0	0	0	0	0	0	0
Measles - 20th week	0	0	0	0	0	0	0
Measles - 24th week	0	0	0	0	0	0	0
Measles - 28th week	0	0	0	0	0	0	0
Measles at 18th to 28th weeks	0	0	0	0	0	0	0
Measles - 32nd week	0	0	0	0	0	0	0
Measles - 36th week	1	1	100.0	0	0	0	0
Measles - 40th week	1	1	100.0	0	0	0	0
Measles at 28th to 40th weeks	2	2	100.0	0	0	0	0
Measles, date of onset N.S.	0	0	0	0	0	0	0
All Measles cases	8	4	50.0	4	50.0	0	0

(c) ALL LIVERBORN INFANTS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases
Control series	5,611	5,431	96.8	156	2.8	24	0.4
Measles up to 4th week	9	8	88.9	1	11.1	0	0
Measles - 4th week	14	11	78.6	3	21.4	0	0
Measles - 8th week	13	12	92.3	1	7.7	0	0
Measles up to 12th week	36	31	86.1	5	13.9	0	0
Measles - 16th week	8	7	87.5	1	12.5	0	0
Measles - 20th week	13	12	92.3	1	7.7	0	0
Measles - 24th week	15	15	100.0	0	0	0	0
Measles - 28th week	8	8	100.0	0	0	0	0
Measles at 18th to 28th weeks	45	42	93.3	3	6.7	0	0
Measles - 32nd week	9	9	100.0	0	0	0	0
Measles - 36th week	9	8	88.9	1	11.1	0	0
Measles - 40th week	2	2	100.0	0	0	0	0
Measles at 28th to 40th weeks	30	29	96.7	1	3.3	0	0
Measles, date of onset N.S.	0	0	0	0	0	0	0
All Measles cases	101	92	91.1	8	7.9	1	1.0

(d) INFANTS ALIVE AT 2 YEARS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases
Control series	5,315	5,234	98.5	81	1.5	0	0
Measles up to 4th week	7	7	100.0	0	0	0	0
Measles - 4th week	11	10	90.9	1	9.1	0	0
Measles - 8th week	11	11	100.0	0	0	0	0
Measles up to 12th week	29	28	96.6	1	3.4	0	0
Measles - 16th week	8	7	87.5	1	12.5	0	0
Measles - 20th week	13	12	92.3	1	7.7	0	0
Measles - 24th week	15	15	100.0	0	0	0	0
Measles - 28th week	8	8	100.0	0	0	0	0
Measles at 18th to 28th weeks	44	42	95.5	2	4.5	0	0
Measles - 32nd week	9	9	100.0	0	0	0	0
Measles - 36th week	8	8	100.0	0	0	0	0
Measles - 40th week	1	1	100.0	0	0	0	0
Measles at 28th to 40th weeks	18	18	100.0	0	0	0	0
Measles, date of onset N.S.	0	0	0	0	0	0	0
All Measles cases	91	88	96.7	3	3.3	0	0

(e) INFANTS ALIVE AT 3 YEARS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases	Infants without major malformation	Infants with major malformation	No. of cases
Control series	5,315	5,234	98.5	81	1.5	0	0
Measles up to 4th week	7	7	100.0	0	0	0	0
Measles - 4th week	11	10	90.9	1	9.1	0	0
Measles - 8th week	11	11	100.0	0	0	0	0
Measles up to 12th week	29	28	96.6	1	3.4	0	0
Measles - 16th week	8	7	87.5	1	12.5	0	0
Measles - 20th week	13	12	92.3	1	7.7	0	0
Measles - 24th week	15	15	100.0	0	0	0	0
Measles - 28th week	8	8	100.0	0	0	0	0
Measles at 18th to 28th weeks	44	42	95.5	2	4.5	0	0
Measles - 32nd week	9	9	100.0	0	0	0	0
Measles - 36th week	8	8	100.0	0	0	0	0
Measles - 40th week	1	1	100.0	0	0	0	0
Measles at 28th to 40th weeks	18	18	100.0	0	0	0	0
Measles, date of onset N.S.	0	0	0	0	0	0	0
All Measles cases	91	88	96.7	3	3.3	0	0

Table L (contd.)

(a) CHICKENPOX

(a) ALL INFANTS

(a) INFANTS BORN DEAD

(c) ALL LIVESBORN INFANTS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	Not stated	No.	%	
Control series	5,611	5,431	96.8	156	2.8	24	0.4
Chickenpox up to 4th week	19	19	100.0	0	0	0	0
Chickenpox - 8th week	31	28	90.3	3	9.7	2	6.5
Chickenpox - 12th week	23	23	100.0	0	0	0	0
Chickenpox up to 12th week	71	70	98.6	1	1.4	2	2.7
Chickenpox - 16th week	21	21	100.0	0	0	0	0
Chickenpox - 20th week	38	37	97.4	1	2.6	0	0
Chickenpox - 24th week	36	34	94.4	2	5.6	0	0
Chickenpox - 28th week	41	39	95.2	2	4.9	0	0
Chickenpox at 13th to 28th weeks	142	137	96.5	4	2.8	1	0.7
Chickenpox - 32nd week	37	36	97.3	1	2.7	0	0
Chickenpox - 36th week	26	25	96.2	1	3.8	0	0
Chickenpox - 40th week	14	14	100.0	0	0	0	0
Chickenpox at 29th to 40th weeks	77	75	97.4	2	2.6	0	0
Chickenpox, date of onset N.S.	1	1	100.0	0	0	0	0
All Chickenpox cases	293	283	96.6	7	2.4	3	1.0

(d) INFANTS BORN ALIVE BUT DYING UNDER 2 YEARS

(d) INFANTS ALIVE AT 2 YEARS

Control series	140	92	65.7	47	33.6	1	0.7
Chickenpox up to 4th week	1	1	100.0	0	0	0	0
Chickenpox - 8th week	1	1	100.0	0	0	0	0
Chickenpox - 12th week	0	0	0	0	0	0	0
Chickenpox up to 12th week	2	2	100.0	0	0	0	0
Chickenpox - 16th week	0	0	0	0	0	0	0
Chickenpox - 20th week	1	1	100.0	0	0	0	0
Chickenpox - 24th week	1	1	100.0	0	0	0	0
Chickenpox - 28th week	1	1	100.0	0	0	0	0
Chickenpox at 13th to 28th weeks	3	3	100.0	0	0	0	0
Chickenpox - 32nd week	0	0	0	0	0	0	0
Chickenpox - 36th week	1	1	100.0	0	0	0	0
Chickenpox - 40th week	1	1	100.0	0	0	0	0
Chickenpox at 29th to 40th weeks	2	2	100.0	0	0	0	0
Chickenpox, date of onset N.S.	0	0	0	0	0	0	0
All Chickenpox cases	7	3	42.9	4	57.1	0	0

No. of cases	Infants without major malformation	Infants with major malformation	Not stated	No.	%	
5,435	5,326	97.6	128	2.3	1	0.0
19	19	100.0	0	0	0	0
29	28	96.6	1	3.4	0	0
23	23	100.0	0	0	0	0
70	69	98.6	1	1.4	0	0
27	27	100.0	0	0	0	0
38	37	97.4	1	2.6	0	0
35	34	97.1	1	2.9	0	0
40	39	97.5	1	2.5	0	0
140	137	97.9	3	2.1	0	0
37	36	97.3	1	2.7	0	0
26	25	96.2	1	3.8	0	0
14	14	100.0	0	0	0	0
77	75	97.4	2	2.6	0	0
1	1	100.0	0	0	0	0
288	282	97.9	6	2.1	0	0

No. of cases	Infants without major malformation	Infants with major malformation	Not stated	No.	%	
5,315	5,234	98.5	81	1.5	0	0
18	18	100.0	0	0	0	0
28	27	96.4	1	3.6	0	0
22	22	100.0	0	0	0	0
68	67	98.5	1	1.5	0	0
27	27	100.0	0	0	0	0
37	37	100.0	0	0	0	0
34	34	100.0	0	0	0	0
39	39	100.0	0	0	0	0
137	137	100.0	0	0	0	0
37	36	97.3	1	2.7	0	0
25	25	100.0	0	0	0	0
13	13	100.0	0	0	0	0
75	74	98.7	1	1.3	0	0
1	1	100.0	0	0	0	0
281	279	99.3	2	0.7	0	0

Table L (contd.)

(a) ALL INFANTS				(b) INFANTS BORN DEAD				(c) ALL LIVEBORN INFANTS			
Type of case	No. of cases	Infants without major malformation	Infants with major malformation	Not stated	No.	%	No.	No. of cases	Infants without major malformation	Infants with major malformation	Not stated
Control series	5,611	5,431	156	24	0.4	0.4	28	17.9	23	14.7	—
Mumps up to 4th week	19	19	0	0	0	0	0	0	0	0	0
Mumps 4th to 12th week	34	32	2	0	2.9	2.9	0	0	0	0	0
Mumps 12th to 20th week	42	41	1	0	1.6	1.6	0	0	0	0	0
Mumps up to 12th week	115	112	3	0	0.9	0.9	0	0	0	0	0
Mumps 16th week	55	52	3	0	1.8	1.8	0	0	0	0	0
Mumps 20th week	50	47	3	0	2.0	2.0	0	0	0	0	0
Mumps 24th week	49	46	3	0	1.4	1.4	0	0	0	0	0
Mumps 28th week	56	53	3	0	1.8	1.8	0	0	0	0	0
Mumps at 13th to 28th weeks	230	218	12	0	1.7	1.7	2	33.3	4	66.7	—
Mumps 32nd week	48	46	2	0	4.2	4.2	0	0	0	0	0
Mumps 36th week	60	59	1	0	1.7	1.7	0	0	0	0	0
Mumps 40th week	19	17	2	0	5.3	5.3	0	0	0	0	0
Mumps at 29th to 40th weeks	147	142	5	0	3.4	3.4	0	0	0	0	0
Mumps, date of onset N.S.	4	4	0	0	0	0	0	0	0	0	0
All Mumps cases	496	477	19	0	1.2	1.2	2	22.2	6	66.7	—

(d) INFANTS BORN ALIVE BUT DYING UNDER 2 YEARS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	Not stated
Control series	140	92	47	1
Mumps up to 4th week	0	0	0	0
Mumps 4th to 12th week	0	0	0	0
Mumps 12th to 20th week	1	1	0	0
Mumps 20th week	0	0	0	0
Mumps 24th week	3	3	0	0
Mumps 28th week	2	2	0	0
Mumps at 13th to 28th weeks	7	4	3	0
Mumps 32nd week	1	1	0	0
Mumps 36th week	2	2	0	0
Mumps 40th week	4	4	0	0
Mumps at 29th to 40th weeks	2	2	0	0
Mumps, date of onset N.S.	0	0	0	0
All Mumps cases	12	7	5	0

(e) INFANTS ALIVE AT 2 YEARS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	Not stated
Control series	5,315	5,234	81	1.5
Mumps up to 4th week	19	19	0	0
Mumps 4th to 12th week	32	31	1	3.1
Mumps 12th to 20th week	61	60	1	1.6
Mumps 20th week	112	110	2	1.8
Mumps 24th week	54	52	2	3.7
Mumps 28th week	46	46	0	0
Mumps at 13th to 28th weeks	64	64	0	0
Mumps 32nd week	53	52	1	1.9
Mumps 36th week	217	214	3	1.4
Mumps 40th week	67	66	1	1.5
Mumps at 29th to 40th weeks	58	58	0	0
Mumps, date of onset N.S.	142	140	2	1.4
All Mumps cases	4	4	0	0
All Mumps cases	475	469	6	1.3

Table L (contd.)

(c) POLIO MYELITIS

(b) ALL INFANTS

(a) INFANTS BORN DEAD

(d) ALL LIVERBORN INFANTS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	Infants with major malformation	Infants without major malformation	Not stated
Control series	5,411	5,431	96.6	156	2.8	24
Poliomyelitis up to 4th week	1	1	—	0	—	0
Poliomyelitis - 4th week	2	2	—	0	—	0
Poliomyelitis - 8th week	3	3	40.0	1	20.0	2
Poliomyelitis up to 12th week	8	5	62.5	1	12.5	2
Poliomyelitis - 16th week	10	10	100.0	0	—	0
Poliomyelitis - 20th week	7	7	100.0	0	—	0
Poliomyelitis - 24th week	7	7	100.0	0	—	0
Poliomyelitis - 28th week	0	0	—	0	—	0
Poliomyelitis at 13th to 28th weeks	24	24	100.0	0	—	0
Poliomyelitis - 32nd week	0	0	—	0	—	0
Poliomyelitis - 36th week	0	0	—	0	—	0
Poliomyelitis - 40th week	0	0	—	0	—	0
Poliomyelitis at 29th to 40th weeks	0	0	—	0	—	0
Poliomyelitis, date of onset N.S.	0	0	—	0	—	0
All Poliomyelitis cases	32	29	90.6	1	3.1	2

(e) INFANTS BORN ALIVE BUT DYING UNDER 2 YEARS

(f) INFANTS ALIVE AT 2 YEARS

Type of case	No. of cases	Infants without major malformation	Infants with major malformation	Infants with major malformation	Infants without major malformation	Not stated
Control series	140	92	65.7	47	33.6	1
Poliomyelitis up to 4th week	0	0	—	0	—	0
Poliomyelitis - 4th week	0	0	—	0	—	0
Poliomyelitis - 8th week	1	1	100.0	0	—	0
Poliomyelitis up to 12th week	1	1	100.0	0	—	0
Poliomyelitis - 16th week	0	0	—	0	—	0
Poliomyelitis - 20th week	0	0	—	0	—	0
Poliomyelitis - 24th week	1	1	100.0	0	—	0
Poliomyelitis - 28th week	0	0	—	0	—	0
Poliomyelitis at 13th to 28th weeks	1	1	100.0	0	—	0
Poliomyelitis - 32nd week	0	0	—	0	—	0
Poliomyelitis - 36th week	0	0	—	0	—	0
Poliomyelitis - 40th week	0	0	—	0	—	0
Poliomyelitis at 29th to 40th weeks	0	0	—	0	—	0
Poliomyelitis, date of onset N.S.	0	0	—	0	—	0
All Poliomyelitis cases	2	1	50.0	1	50.0	0

Table L (contd.)

(a) ALL INFANTS					(b) INFANTS BORN DEAD					(c) ALL LIVEBORN INFANTS						
Type of case	No. of cases	Infants without major malformation %	Infants with major malformation %	Not stated %	No. of cases	Infants without major malformation %	Infants with major malformation %	Not stated %	No. of cases	Infants without major malformation %	Infants with major malformation %	Not stated %				
Control series ..	5,611	5,431	96.8	156	2.8	24	0.4	105	67.4	28	17.9	23	14.7			
Influenza up to 4th week	5	5	100.0	0	0	0	0	0	0	0	0	0	0			
Influenza -8th week	20	20	100.0	0	0	0	0	0	0	0	0	0	0			
Influenza -12th week	16	16	100.0	0	0	0	0	0	0	0	0	0	0			
Influenza up to 12th week ..	41	41	100.0	0	0	0	0	0	0	0	0	0	0			
Influenza -16th week	21	21	95.5	1	4.5	0	0	1	—	0	—	0	—			
Influenza -20th week	28	28	92.9	2	7.1	0	0	0	—	0	—	0	—			
Influenza -24th week	24	24	92.5	2	7.5	0	0	0	—	0	—	0	—			
Influenza -28th week	23	21	91.3	2	8.7	0	0	0	—	0	—	0	—			
Influenza at 13th to 24th weeks	99	92	91.9	7	7.1	0	0	1	—	0	—	0	—			
Influenza -32nd week	14	14	100.0	0	0	0	0	0	—	0	—	0	—			
Influenza -36th week	8	8	100.0	0	0	0	0	0	—	0	—	0	—			
Influenza -40th week	3	3	—	0	0	0	0	0	—	0	—	0	—			
Influenza at 29th to 40th weeks	25	25	100.0	0	0	0	0	0	—	0	—	0	—			
Influenza, date of onset N.S.	0	0	—	0	0	0	0	0	—	0	0	0	—			
All influenza cases ..	165	158	95.8	7	4.3	0	—	2	1	1	—	0	—			
										163	157	96.3	6	3.7	0	—

(d) INFANTS BORN ALIVE BUT DYING UNDER 2 YEARS

Control series	140	92	65.7	47	33.6	1	0.7	5,315	5,234	98.5	81	1.5	0	—
Influenza up to 4th week	0	0	—	0	—	0	—	5	5	100.0	0	—	0	—
Influenza -8th week	0	1	—	0	—	0	—	19	19	100.0	0	—	0	—
Influenza -12th week	0	1	—	0	—	0	—	16	16	100.0	0	—	0	—
Influenza up to 12th week ..	1	1	—	0	—	0	—	40	40	100.0	0	—	0	—
Influenza -16th week	0	0	—	0	—	0	—	21	20	95.2	1	4.8	0	—
Influenza -20th week	1	1	—	0	—	0	—	27	25	92.6	2	7.4	0	—
Influenza -24th week	1	1	—	0	—	0	—	24	23	95.8	1	4.2	0	—
Influenza -28th week	3	2	—	1	33.3	0	—	20	19	95.0	1	5.0	0	—
Influenza at 13th to 24th weeks	5	4	80.0	1	20.0	0	—	92	87	94.6	5	5.4	0	—
Influenza -32nd week	0	0	—	0	—	0	—	14	14	100.0	0	—	0	—
Influenza -36th week	0	0	—	0	—	0	—	8	8	100.0	0	—	0	—
Influenza -40th week	0	0	—	0	—	0	—	3	3	—	0	—	0	—
Influenza at 29th to 40th weeks	0	0	—	0	—	0	—	25	25	100.0	0	—	0	—
Influenza, date of onset N.S.	0	0	—	0	—	0	—	0	0	—	0	—	0	—
All influenza cases	6	5	83.3	1	16.7	0	—	157	152	96.8	5	3.2	0	—

Table M. Numbers and proportions of infants with and without major malformation in the control and rubella series according to parity of mother (rubella up to 12th week shown separately)

Type of case	Number of previous pregnancies	No. of cases	Infants without major malformation		Infants with major malformation		Not stated	
			No.	%	No.	%	No.	%
Control series	0	2,026	1,964	97.0	49	2.4	13	0.6
	1	1,636	1,592	97.3	41	2.5	3	0.2
	2	957	919	96.0	35	3.7	3	0.3
	3	462	447	96.8	13	2.8	2	0.4
	4	239	227	95.0	10	4.2	2	0.8
	5	115	108	93.9	6	5.2	1	0.9
	6	63	63	100.0	0	—	0	—
	7	35	34	97.1	1	2.9	0	—
	8 and over	71	70	98.6	1	1.4	0	—
	Not stated	7	7	100.0	0	—	0	—
	All parities	5,611	5,431	96.8	156	2.8	24	0.4
Rubella up to 12th week	0	69	61	88.4	8	11.6	0	—
	1	47	37	78.7	8	17.0	2	4.3
	2	38	29	76.3	9	23.7	0	—
	3	16	15	93.7	1	6.3	0	—
	4	17	15	88.2	2	11.8	0	—
	5	4	3	—	1	—	0	—
	6	1	0	—	1	—	0	—
	7	0	0	—	0	—	0	—
	8 and over	0	0	—	0	—	0	—
	All parities	192	160	83.4	30	15.6	2	1.0
All rubella cases	0	189	177	93.7	12	6.3	0	—
	1	126	114	90.5	10	7.9	2	1.6
	2	124	113	91.1	11	8.9	0	—
	3	65	62	95.4	3	4.6	0	—
	4	40	37	92.5	3	7.5	0	—
	5	13	12	92.3	1	7.7	0	—
	6	4	3	—	1	—	0	—
	7	1	1	—	0	—	0	—
	8 and over	5	5	100.0	0	—	0	—
	All parities	567	524	92.4	41	7.2	2	0.4

This table excludes all cases delivered up to the 28th week of pregnancy.

Table N. Numbers and proportions of infants with and without major malformation in the control and rubella series according to age of mother (rubella up to 12th week shown separately)

Type of case	Age-group of mother (in years)	No. of cases	Infants without major malformation		Infants with major malformation		Not stated	
			No.	%	No.	%	No.	%
Control series	15-19	269	261	97.0	7	2.6	1	0.4
	20-24	1,591	1,555	97.7	28	1.8	8	0.5
	25-29	1,837	1,765	96.1	62	3.4	10	0.5
	30-34	1,161	1,123	96.7	38	3.3	0	—
	35-39	568	548	96.4	18	3.2	2	0.4
	40-44	156	152	97.4	2	1.3	2	1.3
	45 and over	7	7	100.0	0	—	0	—
	Not stated	22	20	91.0	1	4.5	1	4.5
	All ages	5,611	5,431	96.8	156	2.8	24	0.4
Rubella up to 12th week	15-19	12	11	91.7	1	8.3	0	—
	20-24	71	60	84.5	10	14.1	1	1.4
	25-29	52	39	75.0	12	23.1	1	1.9
	30-34	34	31	91.2	3	8.8	0	—
	35-39	20	16	80.0	4	20.0	0	—
	40-44	3	3	—	0	—	0	—
	45 and over	0	0	—	0	—	0	—
	Not stated	0	0	—	0	—	0	—
	All ages	192	160	83.4	30	15.6	2	1.0
All rubella cases	15-19	34	33	97.1	1	2.9	0	—
	20-24	179	165	92.2	13	7.3	1	.5
	25-29	165	147	89.1	17	10.3	1	.6
	30-34	117	112	95.7	5	4.3	0	—
	35-39	60	55	91.7	5	8.3	0	—
	40-44	8	8	100.0	0	—	0	—
	45 and over	4	4	—	0	—	0	—
	Not stated	0	0	—	0	—	0	—
	All ages	567	524	92.4	41	7.2	2	.4

This table excludes cases delivered up to the 28th week of pregnancy.

APPENDIX 2

RECORD CARD

MINISTRY OF HEALTH ENQUIRY INTO VIRUS INFECTIONS DURING PREGNANCY

(Rubella, Measles, Chickenpox, Mumps, Poliomyelitis)

PART A. To be completed for mother.

1. Local Health Authority (County or County Borough) _____
2. Date of Selection as a virus infection or control _____ / _____ / 19 _____
3. Mother's Surname _____ Full Christian Names _____
4. Mother's date of birth _____ / _____ / 19 _____
5. Address _____
District C.B. 1 Met. B. 2 M.B. or U.D. 3 R.D. 4
6. New address (if changed during course of enquiry) _____
7. Date of Last Monthly Period (1st day) _____ / _____ / 19 _____
8. Number of previous pregnancies _____
9. Virus Infections during this pregnancy.

	(a) Infection occurrence by X	(b) Confirmed by Doctor (indicate by X and state whether mild, moderate or severe)	(c) Date of Onset	(d) Which week of pregnancy
Rubella				
Measles				
Chickenpox				
Mumps				
Poliomyelitis				

10. Date of delivery or abortion (Abortion includes miscarriage) _____ / _____ / 19 _____
11. Duration of gestation in weeks (from 1st day of L.M.P.) _____
12. Place of delivery Home 1 Institution 2
13. Number of children delivered from this pregnancy Alive _____
Stillborn or aborted _____

NOTE—The other side of this form is to be completed for each child delivered whether live or stillborn or aborted (using additional forms when necessary).

LEAVE THIS COLUMN BLANK

1	2
3	4
5	6
7	8
9	10

MINISTRY OF HEALTH

ENQUIRY INTO VIRUS INFECTIONS DURING PREGNANCY

PART B. Complete one copy for each live and stillbirth.

LEAVE THIS
COLUMN BLANK

14. Child's Surname _____ Full Christian Names _____

15. Sex. Male 1 Female 2 16. Birth weight _____ lbs _____ ozs

17. Medical Report at birth Alive 1 Stillborn or aborted 2

18. Congenital defects observed Date of Examination ____ / ____ / 19 ____

(a) _____

(b) _____

(c) _____

Medical Report at 1 year Date of Examination ____ / ____ / 19 ____

19. Additional congenital defects observed

(a) _____

(b) _____

Medical Report at 2 years Date of Examination ____ / ____ / 19 ____

20. Additional congenital defects observed

(a) _____

(b) _____

For child dying under 2 years Date of Death ____ / ____ / 19 ____

21. Age at death (enter in one space only) _____ mins. _____ days
_____ hours _____ months

22. Cause of death as stated on death certificate (or cause of stillbirth or abortion if known.) _____

APPENDIX 3

Rubella cases selected in certain areas in 1953

(a) Outcome of Pregnancies and survival of infants according to time of onset of rubella

Time of onset of Rubella	Total cases	Abortion		Still birth		Liveborn, Died under 2 yrs.		Alive at 2 yrs.	
		No.	%	No.	%	No.	%	No.	%
Rubella up to 12th week	21	2	10	1	5	2	10	16	75
Rubella at 13th to 28th week ..	38	1	3	0	0	1	3	36	94
Rubella at 29th to 40th week ..	6	0	0	0	0	0	0	6	100
All rubella cases	65	3	5	1	2	3	5	58	88

(b) Proportion of infants in which major congenital malformations were recorded, according to time of onset of rubella

(i) All Liveborn Infants

Time of onset of Rubella	Total cases	With major defect		Without major defect	
		No.	%	No.	%
Rubella up to 12th week	18	2	11	16	89
Rubella at 13th to 28th week ..	37	0	0	37	100
Rubella at 29th to 40th week ..	6	0	0	6	100
All rubella cases	61	2	3	59	97

(ii) Infants surviving to 2 years

Time of onset of Rubella	Total cases	With major defect		Without major defect	
		No.	%	No.	%
Rubella up to 12th week	16	1	6	15	94
Rubella at 13th to 28th week ..	36	0	0	36	100
Rubella at 29th to 40th week ..	6	0	0	6	100
All rubella cases	58	1	2	57	98

Special examination at 3-4 years of age

Cases examined	With deafness	
	No.	%
10	3	33
12	0	0

(c) Details of cases of abortion, still birth, infant death and congenital defect

Case No.	Week in pregnancy when rubella occurred			Mother's age	Previous pregnancies	Gestation period in weeks	Birth weight lb. oz.	Defects noted and cause if died	Survival
	0-12th	13th-28th	29th-40th						
<i>Abortions</i>									
53/1	0			21	N.S.	27	—	—	Abortion
53/2	8th			29	0	18	—	—	Abortion
53/3		13th		23	1	14	—	—	Abortion
<i>Still birth</i>									
53/4	8th			29	3	41	8 0	No defect; macerated. Cause: intrauterine asphyxia	Still born
<i>Live born infants with major malformations</i>									
53/6	5th			34	2	42	6 0	Deformity, left foot. Died from congenital heart lesion	Died aged 12 days
53/5	11th			23	1	41	6 8	Mental retardation. ? defective hearing, mild talipes equinovarus. (Found at later, special exam. to have mental deficiency and severe deafness—3 years)	Lived
<i>Infants who died with no defects recorded</i>									
53/7	7th			20	1	40	7 15	Died from broncho-pneumonia	Died aged 2 months
53/8		28th		22	1	40	6 6	Died from otitis media and acute bronchitis	Died aged 8 months
<i>Infants with "suspicious" defects</i>									
53/9		19th		40	6	42	5 0	Soft systolic murmur. Late in walking and talking	Lived
53/10		21st		26	3	40	7 0	Faint systolic murmur	Lived
<i>Infants with hearing defects discovered at special examinations at 3-4 years of age</i>									
53/11	4th			28	2	41	4 14	Marked low tone deafness, both ears. Attending special educational clinic for deaf children (At 4 years old)	
53/12	12th			32	5	42	8 0	Moderate bilateral deafness found at 3½ years. Ordinary school	
53/13	12th			38	2	40	7 0	Severe unilateral deafness found at 3 years. Ordinary school	

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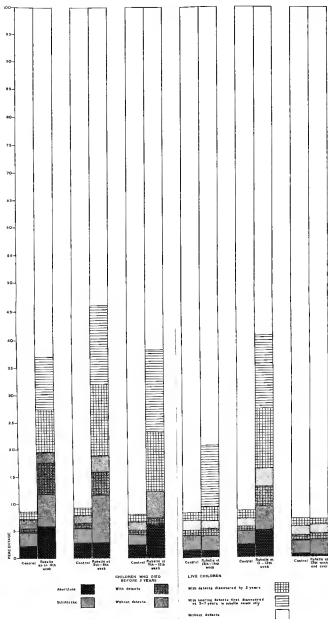


Figure 4. Outcome of 100 control and rubella pregnancies